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ORIGINAL ARTICLE

A prospective study of 728 cases of non-Hodgkin lymphoma from a single laboratory in Shanghai, China

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Abstract The frequency of subtypes of lymphoid neoplasms was determined in a prospective series of 831 patients presenting at 29 Shanghai hospitals over a 4-year period. Diagnosis and classification was established in a single laboratory according to the 2001 WHO classification system. The frequency of non-Hodgkin lymphoma was 87.6% ($n = 728$) and Hodgkin lymphoma was 12.4% ($n = 103$). The most prevalent NHL subtypes diagnosed using WHO criteria were diffuse large B cell lymphoma (DLBCL), precursor B lymphoblastic leukemia/lymphoma and chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). Although a low incidence has been reported in some Asian populations, CLL/SLL was commonly encountered, indicating that chronic lymphoid neoplasms are not rare in Shanghai. Consistent with previous reports, our findings indicate a decrease in the frequency of follicular lymphoma and an increase in T cell neoplasms compared to the West. Precursor T lymphoblastic leukemia/lymphoma, anaplastic large T cell lymphoma, aggressive NK cell leukemia, angioimmunoblastic T cell lymphoma and peripheral T cell lymphoma were prominent subtypes of T cell NHL.

Keywords Non-Hodgkin lymphoma · 2001 WHO diagnostic criteria · Prospective study

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1 Introduction

Non-Hodgkin lymphoma (NHL) refers to more than two dozen distinct neoplastic diseases of the lymphoid system that involve the malignant outgrowth of B and T lymphocytes. The individual characteristics of different lymphomas are thought to result from the neoplastic transformation of different lymphocytic populations at different stages in their maturation and transformation [1]. Over the last two decades, advances in knowledge of the biology of NHL have resulted in the development of an international consensus for the diagnosis and classification of NHL and its subtypes. The World Health Organization (WHO) Classification of Tumors of Hematopoietic and Lymphoid Tissues [2] was put forth in 2001 in order to provide uniform diagnostic criteria for NHL subtypes on

the basis of morphology, immunophenotype, cytogenetics, pathogenesis and clinical characteristics. The WHO classification is based on and extends the 1994 Revised European American Lymphoma (REAL) classification system [3]. The WHO classification recognizes three major categories of lymphoid neoplasms: B cell neoplasms, T and NK cell neoplasms and Hodgkin lymphoma. However, in contrast to REAL, lymphoid leukemias also are included in the WHO classification which stratifies lymphoid neoplasms on the basis of cellular origin and biology [2].

To date, the use of the WHO classification in studies of NHL in China have been limited by the lack of uniform access to the diagnostic tools (e.g., immunohistochemistry, cytogenetics, fluorescence in situ hybridization (FISH)) required to meet WHO criteria. Reports from previous epidemiologic studies using the REAL classification system have indicated significant differences in the prevalence of NHL subtypes between Asia and the West. For example, follicular lymphoma constitutes 22% of NHL in the US but is reported to represent only 5% of NHL in China [4]. The prevalence of follicular lymphoma and prolymphocytic NHL in Japan are also less than in the West while diffuse large B cell and lymphoblastic NHL are higher [5]. In Korea as well, extranodal diffuse large B cell and angioimmunoblastic T cell NHL are higher than in the West [6]. In contrast to the US, NHL of T cell origin is almost twice as prevalent in China, Japan and Korea [7]. Conflicting results have been reported for the prevalence of CLL/SLL in Asian and Western populations [8]. CLL is the most common chronic lymphoproliferative disorder in the West accounting for approximately 25–38% of all leukemias. Alternatively, previous studies have reported the incidence of CLL in Asian populations (e.g., Chinese, Japanese and Singapore Chinese) to be 12–20 times lower, occurring in only 1.2–2% of Eastern patients. However, Kwong and colleagues [9] found that CLL represents 12.5% of all leukemias diagnosed in Hong Kong over a 3-year period. The etiology of NHL is complex. Genetics, immunologic or other neoplastic diseases, as well as infectious agents, including viruses such as Epstein–Barr virus (EBV), Hepatitis B and C virus, and Human Immunodeficiency virus (HIV), appear to influence differences in the prevalence of NHL worldwide [10–13].

The object of this study was to diagnose and classify all lymphoid neoplasms that presented over a 4-year period in a single diagnostic laboratory in Shanghai, China. A total of 831 consecutive cases of lymphoid neoplasms met criteria for diagnosis and classification according to WHO. Herein, we present and compare distribution of NHL subtypes obtained in our prospective series with a recent report of retrospective classification of lymphoid tumors in China using WHO criteria [14]. We also include patient demographics, laboratory values, viral serology and cytogenetic data for the major NHL subtypes diagnosed in our laboratory.

2 Materials and methods

2.1 Case series

Patients $\geq$18 years presenting at Shanghai hospitals between August 2003 and May 2007 were referred to our laboratory based on initial clinical presentation. Protocol approval for this case review was obtained by the Combined Multiple Institutional Review Board of the University of Colorado at Denver and Health Sciences Center in Denver, CO and the Internal Review Board at Fudan University in Shanghai, China.

2.2 Sample collection and clinical laboratory analysis

Peripheral blood, bone marrow aspirates, tissue and core biopsies were collected in conjunction with diagnostic procedures and were evaluated in our laboratory. Peripheral blood smears were obtained by finger stick. Blood samples were collected by venipuncture and processed for routine CBC (CellDyne 3700, Abbott, Park, IL), viral serology (HCV and HIV) (Imx, Abbott) and clinical chemistry for liver enzymes (LDH, ALT and AST enzymes) (COBAS, Integra 400 plus, Roche Diagnostics, Shanghai, China).

2.3 Morphology

Bone marrow aspirates and core biopsies were obtained by Jamshidi needle extraction from the posterior iliac crest, while lymph node and tissue biopsies were obtained by surgical resection. Bone marrow smears were prepared and evaluated using Wright–Giemsa stained preparations and special stains. A broad panel of antibodies were used for immunophenotyping of bone marrow and lymphoid cells by either dual laser flow cytometry (FC-500, Beckman Coulter, Hialeah, FL; Immunotech, Miami, FL), immunoperoxidase-immunohistochemistry of tissue sections or both. Biopsy sections were stained with Hematoxylin–Eosin (H&E). Morphology was independently evaluated by three of us (X.-Z. Z., R. D. I., J. R.). Microscopic analysis was performed using Olympus BX51 bright field microscopes (Olympus Optical Ltd., Tokyo, Japan).

2.4 Cytogenetic analysis

Conventional cytogenetic analysis was performed on unstimulated (1–2 day), and B cell mitogen stimulated (3-day) (lipopolysaccharide) (Sigma, St. Louis, MO), cultures

of bone marrow or lymph node preparations. A minimum of 20 metaphases were analyzed in each case. Criteria for a clone and descriptions of karyotype followed the recommendations of the International System for Human Cytogenetic Nomenclature (1995) [15].

2.5 Fluorescence in situ hybridization analysis (FISH)

FISH analysis was performed on bone marrow or lymph node preparations using Vysis probes (Downers Grove, Illinois) to identify *IGH*/14q34, *ALK*/2p23 *CCND1/IGH*/t(11;14), BCL2/IGH/t(14;18) and other abnormalities as required. Sample preparations and hybridizations were conducted following the manufacturer's recommendations. Whenever possible, a minimum of 500 interphase cells were scored for each probe. A clonal aberration was defined as the percentage of cells with any given aberration over the normal cut-off limits that were determined from ten cytogenetically normal individuals.

3 Results

3.1 Total number lymphoid neoplasms diagnosed using WHO classification criteria

A total of 831 consecutive lymphoid neoplasms were diagnosed according to the WHO classification over a 4-year period (Table 1). The percent of B cell neoplasms as compared to T/NK cell neoplasms was 68.4 and 18.2%, respectively. A total of 103 cases of Hodgkin lymphoma were diagnosed, which constituted 12.4% of total lymphoid neoplasms. Using WHO criteria, a total of 728 NHL were diagnosed, including precursor B and T cell leukemias as well as lymphomas (Table 2). B cell NHL composed 78.0% ($n = 568$) of all NHL cases whereas T/NK cell NHL composed 20.7% ($n = 151$) of the total NHL cases diagnosed in our series.

Table 1 Total number of lymphoid neoplasms diagnosed in series by WHO criteria in Shanghai, China over a 4-year period

Total lymphoid neoplasms	$n = 831$	Percent of total (%)
Mature B cell neoplasms	428	51.5
Precursor B lymphoblastic lymphoma	3	< 1
Precursor B lymphoblastic leukemia	137	16.5
Total B cell NHL	568	68.4
Mature T/NK cell neoplasms	105	12.6
Precursor T lymphoblastic lymphoma	21	2.5
Precursor T lymphoblastic leukemia	25	3.0
Total T/NK cell NHL	151	18.2
NHL NOS	9	1.1
Hodgkin lymphoma	103	12.4

3.2 NHL subtypes defined by WHO criteria

B cell NHL was at least 3 times more prevalent than T cell NHL (568 and 151, respectively) (Table 2). The most frequent subtype of B cell NHL diagnosed in our laboratory was diffuse large B cell lymphoma ($n = 212$) followed by precursor B lymphoblastic leukemia/lymphoma ($n = 140$) and then CLL/SLL ($n = 71$), representing 29.1, 19.2 and 9.8% of all NHL diagnosed in our laboratory, respectively. The most commonly diagnosed type of T/NK cell NHL was precursor T lymphoblastic leukemia/lymphoma ($n = 46$) followed by peripheral T cell lymphoma, unspecified ($n = 40$) and angioimmunoblastic T cell lymphoma ($n = 26$). These findings differ somewhat from those of Wang et al. (2005) [14] who reclassified 447 archival specimens of malignant lymphoma presenting at the Shanxi Tumor Hospital in Taiyuan, China, over an 8-year period using the WHO classification. They found diffuse large B cell lymphoma to be the most common NHL subtype (35.1%) followed by peripheral T cell lymphoma, unspecified (12.0%), extranodal marginal zone B cell lymphoma (11.7%) and follicular lymphoma (8.6%). Cases of T/NK cell neoplasms comprised 30.6% of NHL reported for this re-classification.

3.3 Gender and age distribution of NHL subtypes as defined by WHO criteria

The gender and age distribution for NHL cases presenting in our laboratory is displayed in Fig. 1. The overall gender distribution for NHL in our laboratory was approximately 2:1 male to female (443 and 285, respectively). Gender distribution of B cell NHL favored male (60%) over female (40%) and was similar for T/NK cell NHL, male (64%) female (36%). There was a marked male predisposition for CLL/SLL (3:1) and mantle cell lymphoma (3.7:1). Females with precursor B lymphoblastic leukemia slightly outnumbered males (1.06:1). However, when normalized for gender, the prevalence of precursor B lymphoblastic leukemia in females was twice that observed in males. Males with peripheral T cell lymphoma, unspecified (PTCL-u) outnumbered females (1.8:1). However, when normalized for gender the prevalence of PTCL-u was equal in males and females. The median age for all NHL and B cell NHL was 56 and 58 years, respectively. The median age for T/NK cell neoplasms was slightly younger (49 years). Overall there were no obvious differences between males and females for age at presentation with the exception of precursor B lymphoblastic leukemia for which the median

Table 2 Comparison of the distribution of NHL subtypes in China classified according to WHO criteria

	Distribution in Shanghai[a] ($n = 728$) % (n)	Wang et al.[b] ($n = 385$) % (n)
B-cell NHL	78.0 (568)	68.3 (263)
T/NK cell NHL	20.7 (151)	30.6 (119)
NHL NOS	1.2 (9)	
Diffuse large B cell lymphoma	29.1 (212)	35.1 (135)
Precursor B lymphoblastic leukemia[a](137)/ lymphoma[a](3)	19.2 (140)	1.0 (4)
Chronic lymphocytic leukemia[a](29)/ small lymphocytic lymphoma[a](42)	9.8 (71)	3.6 (14)
Follicular lymphoma	7.0 (51)	8.6 (33)
Precursor T lymphoblastic leukemia[a](25)/ lymphoma[a](21)	6.3 (46)	7.0 (27)
Peripheral T cell lymphoma, unspecified	5.5 (40)	12.0 (46)
Angioimmunoblastic T cell lymphoma	3.6 (26)	2.3 (9)
Plasma cell myeloma	2.9 (21)	1.3 (5)
Extranodal marginal zone B cell lymphoma (MALT)	2.5 (18)	11.7 (45)
Anaplastic large cell lymphoma	2.1 (15)	4.2 (16)
Mantle cell lymphoma	1.9 (14)	2.6 (10)
Burkitt lymphoma[a](10)/leukemia[a](2)	1.6 (12)	0.3 (1)
Aggressive NK cell leukemia	1.2 (9)	(0)
Nodal marginal zone B cell lymphoma	1.1 (8)	0.5 (2)
Lymphoplasmacytic lymphoma	0.8 (6)	2.3 (9)
Splenic marginal zone lymphoma	0.7 (5)	0.3 (1)
Extranodal NK/T cell lymphoma	0.6 (4)	1.3 (5)
T cell prolymphocytic leukemia	0.6 (4)	0.5 (2)
B-cell prolymphocytic leukemia	0.6 (4)	0.5 (2)
T cell large granular lymphocytic leukemia	0.6 (4)	(0)
Other NHL subtypes represented at <1%	<2.5 (18)	<1.0 (4)

[a] Diagnosed and classified in series at a single diagnostic laboratory in Shanghai China over a 4-year period ($n = 728$)

[b] Adaptation from Jinfen Wang et al. (2005) [14] ($n = 385$)

age at presentation for males and females was 38 and 47 years, respectively.

3.4 Distribution of NHL cases from Shanghai and nearby provinces

The vast majority of NHL cases presenting were from Shanghai (78.5%) (Table 3), including cases that constitute the most prevalent NHL subtypes diagnosed in our laboratory. We recorded 18 cases of CLL/SLL and DLBCL in patients from neighboring Zhejiang (4 and 14, respectively). Moreover, 47 of our NHL cases came from Jiangsu province (including 5 CLL/SLL and 12 DLBCL). Other than Shanghai, there were no distinct clusters of NHL subtypes associated with a specific province.

3.5 Clinical features associated with NHL subtypes

Clinical findings for the most prevalent B cell and T/NK cell NHL subtypes are illustrated in Table 4. Abnormal mean hematologic values indicated peripheral blood involvement for 8 out of the 13 major NHL subtypes presented. Predictably, NHL cases presenting as leukemia, precursor B lymphoblastic leukemia and precursor T lymphoblastic leukemia, showed hematologic abnormalities in multiple lineages. The LDH index was elevated in 11 NHL subtypes with the highest levels observed for precursor B lymphoblastic leukemia. Histological grading of follicular lymphoma cases was performed based on the absolute number of centroblasts present in neoplastic follicules. These findings indicate that 43% of the follicular lymphoma cases in our laboratory were classified grade 3. Viral serology for hepatitis C virus (HCV) was performed in 509 NHL cases (data not shown). Only five cases were positive for HCV serology: three cases of precursor B lymphoblastic leukemia, one case of angioimmunoblastic T cell leukemia and one case of anaplastic large cell lymphoma. Serology for HIV was measured in cases of NHL, but because individuals testing positive for HIV in China are routinely quarantined, no HIV+ cases of NHL were encountered in this series.

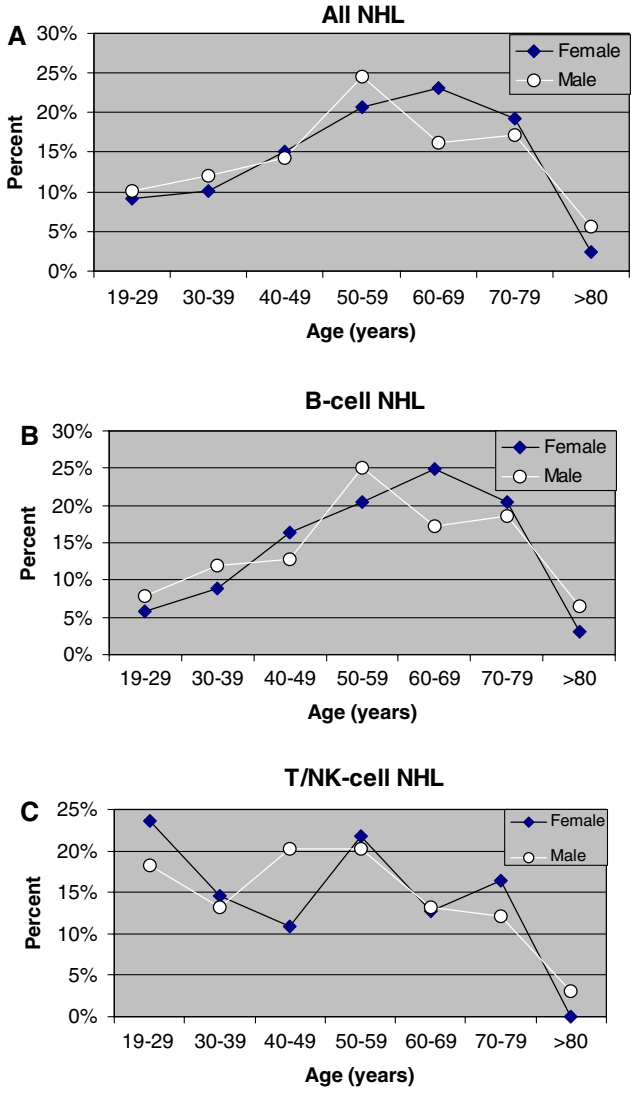

Fig. 1 Age and gender distribution for both males and females diagnosed with **a** All NHL, **b** B cell NHL and **c** T cell NHL in Shanghai, China

3.6 Clonal abnormalities associated with NHL subtypes

Cytogenetic and/or FISH analysis was performed in 724 out of 728 cases of NHL. Informative analysis was obtained in 603 cases and the overall rate for clonal abnormalities in all NHL cases was 81%. Cytogenetic abnormalities for the most prevalent B cell and T/NK cell NHL subtypes are presented in Table 5. The most common cytogenetic abnormality observed in precursor B lymphoblastic leukemia was t(9;22) (37%). Predictably, all follicular lymphomas had clonal cytogenetic abnormalities with complex abnormalities observed in 72% of cases. However, t(14;18) was observed in only 37% of follicular lymphoma cases. Trisomy 12 (+12) was observed in 25% (13/52) of CLL/SLL cases where clonal abnormalities were observed. Overall, complex karyotypes predominated in all NHL subtypes. Whenever possible, genetic aberrations observed in chromosomal analysis were further confirmed by FISH analysis with appropriate probes (Fig. 2).

Table 3 Distribution of NHL cases from Shanghai and nearby provinces

Province	Percent
Shanghai	78.5
Zhejiang	7.5
Jiangsu	6.4
Anhuei	3.3
Jiangxi	1.6
Sichuan	0.7
Other[a]	<2.0

[a] Additional provinces each represented at less than 0.5

4 Discussion

We present 831 consecutive cases of newly diagnosed lymphoid neoplasms evaluated in a single laboratory in Shanghai, China. Patients with suspected lymphoid neoplasms were referred from 29 participating hospitals in the Shanghai area. Prospective diagnosis and disease classification were based on the WHO system (2001) [2]. Consistent with previous reports, our findings indicate that 87.6% of the lymphoid neoplasms are NHL and 12.4% are Hodgkin lymphoma [14]. Of the NHL cases diagnosed in our series, the frequency of B cell NHL is 78.0% and T/NK cell NHL is 20.7%, confirming that although B cell neoplasms predominate, NHL of T/NK cell origin are more frequently encountered in China than in the West [14, 16, 17]. Predictably, there is a general 2:1 predisposition of males over females for all NHL. Notable exceptions were CLL/SLL (male:female = 3:1), mantle cell lymphoma (male:female = 3.7:1) and precursor B lymphoblastic leukemia (male:female = 0.94:1).

Historically, the largest previous Western study of NHL employed the REAL system which classified solid tumors of immature B and T cell origin as lymphoblastic lymphoma. Precursor B and T cell leukemias were evaluated separately as acute lymphoblastic leukemia (ALL). Armitage and colleagues [18] compiled 1,403 cases of NHL diagnosed by REAL from 9 different countries and reported diffuse large B cell lymphoma (31%) was the most common form of B cell neoplasm followed by follicular lymphoma (22%). CLL/SLL, peripheral T cell lymphoma-unspecified, mantle cell lymphoma and extranodal marginal zone B cell lymphoma were all represented relatively equally in the population (5–6%). Lymphoid neoplasms of T cell origin represented only 9–10% of NHL. Similar to

Table 4 Mean laboratory values for the most prevalent NHL subtypes diagnosed in series according to WHO in Shanghai, China in a 4-year period

	ANC (10^9/L)	ALC (10^9/L)	PLT (10^9/L)	Hgb (g/dL)	LDH Index
Diffuse large B cell lymphoma[a](125/212)	3.7	1.4	200.2	12.1	4.7[b]
Precursor B lymphoblastic leukemia[a](137/137)	2.2	18.6[b]	71.0[b]	9.0[b]	4.2[b]
Chronic lymphocytic leukemia/small lymphocytic lymphoma[a](54/71)	2.9	12.7[b]	171.1	11.9[b]	1.1
Follicular lymphoma[a](26/51)	3.7	1.7	207.5	13.3	1.3[b]
Extranodal marginal zone B cell lymphoma (MALT)[a](13/18)	1.9	6.2	135.0	7.7[b]	0.9
Plasma cell myeloma[a](21/21)	2.8	2.7	132.6	6.7[b]	1.2[b]
Mantle cell lymphoma[a](7/14)	3.3	3.9	142.5	11.7[b]	1.3[b]
Peripheral T cell lymphoma, unspecified[a](23/40)	3.1	1.9	176.5	11.2[b]	1.3[b]
Angioimmunoblastic T cell lymphoma[a](16/26)	4.4	1.3	200.0	12.0	1.4[b]
Precursor T lymphoblastic leukemia[a](25/25)	2.2	27.2[b]	124.0	10.2[b]	3.6[b]
Anaplastic large cell lymphoma [a] (8/15)	5.4	6.0	199.0	11.9[b]	2.1[b]
Precursor T lymphoblastic lymphoma [a](5/21)	3.6	2.3	247.4	12.3	1.2[b]
Burkitt lymphoma [a](6/10)	3.8	5.9	240.0	12.0	2.8[b]

Abbreviations and references ranges: absolute neutrophil count (ANC) 2–7 $\times$ 10^9 L^{-1}, absolute lymphocyte count (ALC) 1.6–6 $\times$ 10^9 L^{-1}, platelet count (PLT) 100–300 $\times$ 10^9 L^{-1}, lactate dehydrogenase (LDH) Index = n IU L^{-1}(255 IU L^{-1})$^{-1}$, hemoglobin (Hgb) 12–16 g dL^{-1}

[a] Cases with laboratory values versus total number of cases ()

[b] Indicates abnormal laboratory value

Armitage, diffuse large B cell lymphoma (45%) was the most prevalent NHL subtype diagnosed in our laboratory in Shanghai. However, significant differences were observed between our series and Armitage for CLL/SLL, follicular lymphoma and T cell neoplasms. CLL/SLL was almost 3 times more prevalent in our series (15%), whereas follicular lymphoma represented only 11% in our series compared to 22% in Armitage. Malignant lymphoma of T cell origin was also more prevalent in our series (24%) compared to Armitage (9–10%).

A total of 81% of CLL/SLL presented with structural cytogenetic abnormalities in our series. The most frequently encountered abnormality was trisomy 12 (25%) which is similar to that reported in Western populations ($\sim$20%) [2]. Conflicting reports concerning the prevalence of CLL/SLL in Asia have appeared over the last decade with the prevalence ranging from 3.6% (Wang et al. 2005) to 12.5% (Kwong et al. 1994) [9, 14, 16]. Our findings indicate a relatively high prevalence of CLL/SLL for NHL in Shanghai (9.8 and 15% for WHO and REAL, respectively). A possible explanation for the disparity between these results and some other studies may involve variations in the sampling and/or diagnostic methodologies employed. Historically in China, lymphoid neoplasms presenting as leukemias are more likely to be reported by hematologists, whereas solid lymphoid tumors are more likely to be encountered by pathologists. Therefore, even utilizing WHO 2001 criteria, retrospective studies may have a selection bias based on the source of material sampled for evaluation.

The potential impact of sampling bias is further illustrated by the marked difference in prevalence between precursor B lymphoblastic leukemia in our series (19.2%) compared to Wang et al. (1.0%) [14]. Even though both employed WHO diagnostic criteria, the vast majority of precursor B lymphoblastic leukemia in our series initially presented as hematology cases and not as solid tissue tumors. The majority of studies of precursor B lymphoblastic leukemia focus on children with immature B cell leukemia being the most common form of leukemia diagnosed in the West under the age of 6 years and in youths [19]. However, in the West adult precursor B lymphoblastic leukemia is rarely diagnosed in the general adult population (0.7–1.8/100,000 per year) [20]. Precursor B lymphoblastic leukemia/lymphoma was the second most frequently diagnosed lymphoid neoplasm in our series in Shanghai (n = 140). Taken together, these findings suggest that the adult form of the disease may be under-reported in China. Not only did females predominate in precursor B lymphoblastic leukemia, there was a marked gender difference in the median age at presentation, suggesting possible differences in the etiology or pathogenesis of precursor B lymphoblastic leukemia.

Reflecting the lower prevalence of follicular lymphoma in Asian populations relative to the West, this disease represented only 7% of the NHL in our series based on WHO classification [4, 14, 17, 21–23]. Although, complex cytogenetic abnormalities were observed in virtually all cases analyzed in this series, an explanation for the low frequency of t(14;18) is not immediately apparent.

Table 5 Clonal abnormalities in NHL subtypes diagnosed in series according to WHO in Shanghai, China in a 4-year period

NHL subtype	Patients with informative analysis (%)	Structural abnormalities (%)	Most common abnormality
Diffuse large B cell lymphoma	180/212 (85%)	174/180 (97%)	Abn. 13 (7%)
			t(3;14) (10%)
			6q- (12%)
			t(14;18) (3%)
			IGH rearrangements (26%)
Precursor B lymphoblastic leukemia	114/137 (83%)	87/114 (76%)	t(9;22) (37%)
			+8 (13%)
			−7 (10%)
Chronic lymphocytic leukemia/small lymphocytic lymphoma	64/71 (90%)	52/64 (81%)	+12 (25%)
			IGH rearrangements (21%)
			11q- (11%)
Follicular lymphoma	43/51 (84%)	43/43 (100%)	t(14;18) (37%)
			+7 (6%)
			t(13;14) (8%)
			IGH rearrangements (14%)
			Complex (72%)
Extranodal marginal zone B cell lymphoma	11/18 (61%)	4/11 (36%)	Complex (75%)
Plasma cell myeloma	16/21 (76%)	11/16 (69%)	Complex (82%)
Mantle cell lymphoma	12/14 (86%)	12/12 (100%)	t(11;14) (42%)
Peripheral T cell lymphoma, unspecified	28/40 (70%)	16/28 (57%)	+X (19%)
			del (6) (19%)
			Complex (69%)
Angioimmunoblastic T cell lymphoma	19/26 (73%)	7/19 (37%)	Abn. X or Y (57%)
Precursor T lymphoblastic leukemia	21/25 (84%)	17/21(81%)	Complex (82%)
Anaplastic large cell lymphoma	11/15 (73%)	7/11(64%)	Complex (86%)
Precursor T lymphoblastic lymphoma	16/21 (76%)	11/16 (69%)	Abn. (1)(p36) (27%)
			abn 5 (27%)
			Complex (73%)
Burkitt lymphoma	9/10[a] (90%)	4/9 (44%)	t(8;14) (40%)
			Complex (43%)

Definitions: Abn. Refers to an abnormality in a particular chromosome. Complex refers to a karyotype with greater than two independent cytogenetic lesions. Informative cytogenetic and/or FISH analysis refers to cases with a positive FISH analysis and either a normal karyotype or abnormal karyotype in greater than or equal to 20 metaphases (see Sect. "Materials and methods")

[a] All cases of Burkitt Lymphoma were positive for c-myc by cytogenetics, FISH or immunohistochemistry

Typical of Asia, the frequency of T cell neoplasms in Shanghai is approximately 3 times higher than encountered in Western populations. Surprisingly, rare neoplasms (i.e., anaplastic large T/null cell lymphoma, angioimmunoblastic T cell lymphoma and aggressive NK cell leukemia) together constituted the majority of T cell lymphomas, while peripheral T cell lymphoma was not encountered more often than reported in Western studies [17, 18]. The majority of these tumors exhibited complex karyotypes. EBER positive cells were detected in 63% of angioimmunoblastic T cell lymphoma and in all cases of aggressive NK cell leukemia (a diagnostic criteria for this disease) [24].

NHLs are a heterogeneous group of neoplasms with complex clinical, biological and molecular features. It is becoming increasingly appreciated that significant regional differences in the pattern of NHL subtypes exist that can be attributed to multiple factors, such as infection, family history, genetic predisposition, autoimmune disease, environment, immunosuppression as well as methodologic limitations or artifact. Our findings provide the first prospective basis for comparison of the prevalence of NHL subtypes in Shanghai based on WHO 2001 criteria and serve as a point of departure for future studies to better understand the contribution of multiple influences on the development of these diseases in China.

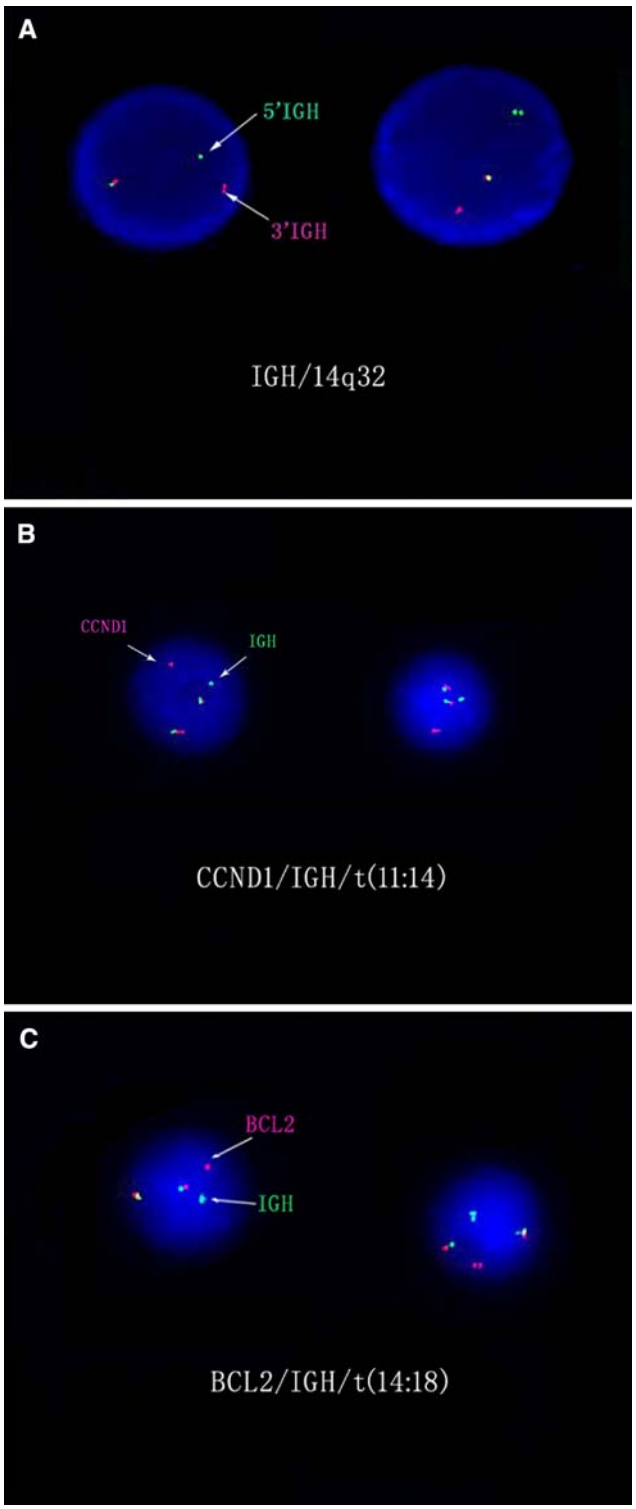

Fig. 2 FISH analysis of IGH fusion genes. **a** FISH using I*GH* BreakApart probe. Fusion signal represents normal; *green* and *red* represent rearranged 5′ and 3′, respectively, of *IGH* locus. **b** FISH with the Dual-fusion and Dual-color *CCND1/IGH* probe. Fusion signals represent fusion genes. **c** FISH with the Dual-fusion and Dual-color *BCL2/IGH* probe. Fusion signals represent fusion genes

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