Chromosomal abnormalities of 200 Chinese patients with non-Hodgkin’s lymphoma in Taiwan: with special reference to T-cell lymphoma

C.-Y. Chen¹, M. Yao¹, J.-L. Tang¹, W. Tsay¹, C.-C. Wang², W.-C. Chou¹, I.-J. Su³, F.-Y. Lee³, M.-C. Liu³ & H.-F. Tien¹,³*

Departments of ¹Internal Medicine, ²Oncology and ³Pathology, National Taiwan University Hospital, Taipei, Taiwan

Received 25 October 2003; revised 11 February 2004; accepted 24 February 2004

Background: The distribution of the histopathological subtypes of non-Hodgkin’s lymphoma (NHL) is different among various geographical areas. However, there are few reports concerning cytogenetic findings of NHL, especially T-cell lymphoma, in Asian people.

Patients and methods: We analyzed the chromosomal abnormalities of 200 adult patients with NHL in Taiwan and correlated the non-random aberrations with the histological subtypes.

Results: One hundred and thirty-eight patients (69%) had B-cell lymphoma. The incidence of the t(14;18) in total lymphoma was lower in Taiwan (12%) than in the West (20–30%), but its incidence in follicular lymphoma was comparable between the two areas (17 of 28 patients, 61% versus 50–60%). Sixty-two patients (31%) had T-cell lymphoma, including 11 angiocentric T/natural killer (NK)-cell lymphoma and only two angioimmunoblastic T-cell lymphoma (AILD). The recurrent chromosomal abnormalities in T-cell lymphoma comprised 6q deletion (30%), 11q deletion (20%), 17p deletion (16%), −Y (14%) and +8 (11%). Angiocentric T/NK-cell lymphoma had a significantly higher frequency of 1q duplication (P = 0.001), 6p duplication (P < 0.001) and 11q deletion (P = 0.011) than other T-cell lymphoma. The incidences of +3 and +5, two common abnormalities in AILD, were quite low in T-cell lymphoma in Taiwan (4% and 2%, respectively), compared with those in the West (16–32% and ~15%, respectively). The 11q deletion, not a common aberration in T-cell lymphoma in western countries, occurred quite frequently in Taiwan.

Conclusions: The chromosomal aberrations of NHL are quite different among various geographical areas, which may reflect the differences in the distribution of the histological subtypes of lymphoma among various areas.

Key words: chromosomal abnormalities, non-Hodgkin’s lymphoma, T-cell lymphoma

Introduction

A number of recurrent chromosomal abnormalities have been identified in non-Hodgkin’s lymphoma (NHL), that correlate with histopathological subtypes and clinical conditions [1]. For example, the t(14;18) is highly associated with follicular lymphoma, the t(8;14) with Burkitt’s lymphoma, the t(11;14) with mantle-cell lymphoma, the t(2;5) with anaplastic large-cell lymphoma, and 3q27 abnormalities with diffuse large B-cell lymphoma [2]. The distribution of the histological subtypes of NHL differs significantly between the East and the West [3, 4]. There are lower frequencies of small lymphocytic lymphoma/chronic lymphocytic leukemia and follicular lymphoma, but higher incidences of peripheral T-cell lymphoma in the East than in the West [5–7]. Some large series studies of chromosomal abnormalities of NHL in western countries have been reported [8–10]. However, there have been few reports of cytogenetic abnormalities in patients with NHL in Asia [11, 12]. The data of chromosomal abnormalities in peripheral T-cell lymphoma are also limited [13, 14]. It is not clear whether the occurrence of the recurrent chromosomal abnormalities in NHL is also different in different geographical areas. In this study, we analyzed the cytogenetic abnormalities in 200 consecutive Chinese patients with NHL in Taiwan. We found that though the incidence of the chromosomal abnormality t(14;18) among all NHL is lower in this area than in western countries (12% versus 20–30%), the frequency of t(14;18) in follicular lymphoma in Taiwan is comparable with...
that in the West (61% versus 50–60%). In addition, some geographical differences in the chromosomal aberrations in T-cell lymphoma were found which might reflect the difference in the distribution of the histopathological subtypes between this area and the West.

Patients and methods

Patient population and tissue samples

The specimens were obtained from 200 consecutive adult patients with NHL in National Taiwan University Hospital between 1985 and 2001. Patient age ranged from 18 to 88 years (median 52). The specimens included lymph nodes (103 patients), bone marrows (60 patients), pleural effusions (14 patients), skin nodules (six patients), nasal masses (four patients), peripheral blood (five patients), spleens (four patients), liver (one patient), stomach (two patients) and breast (one patient). The histopathological examination, immunohistochemical staining and cytogenetics were performed on the same specimen from each individual. The lymphomas were subclassified according to the Revised European–American Lymphoma (REAL) classification (Table 1). One hundred and thirty-eight patients (69%) were diagnosed as having B-cell lymphoma and 62 patients (31%) as having T-cell lymphoma. Patients presenting mainly with leukemia, such as large granular lymphocytic leukemia, and chronic lymphocytic leukemia were not included in this study. The karyotypes of five patients with angiocentric T/natural killer (NK)-cell lymphoma and three patients with hepatosplenic T-g/d lymphoma have been published before [15–17].

Cytogenetic analysis

Cytogenetic analysis was performed as described previously [15]. Briefly, the lymph nodes and/or tumor tissue were minced with surgical blades into small fragments, and the separated cells were washed and set up for 1-day culture before harvest. Bone marrow, pleural effusion and peripheral blood cells were harvested either directly or after 1–3 days of culture. Metaphase chromosomes were banded by the conventional trypsin–Giemsa banding technique and karyotyped according to ISCN [18].

Results

Cytogenetic results of B-cell NHL and their correlation with histopathological subtypes and clinical outcomes

One-hundred and thirty-eight patients (69%) studied had B-cell NHL. The distribution of the histopathological subtypes is shown in Table 1. One-hundred and thirty-four patients had clonal chromosomal abnormalities. The modal chromosome number varied from 43 to 107, most commonly pseudodiploidy (53 cases), followed by hyperdiploidy between 47 and 50 (51 cases). Hypodiploidy was rare (13 cases, 10%). The distribution of non-random chromosomal abnormalities is shown in Table 2. Among the 120 patients with near- or pseudodiploidy, recurrent numerical chromosome aberrations included trisomy 12 (13%), trisomy 3 (11%), trisomy X (9%), trisomy 18 (8%), monosomy 8 (8%), trisomy 7 (7%) and monosomy 13 (4%). Chromosomal rearrangements involving 14q32 were detected in 65 patients (65 of 134, 49%), including those with specific translocation (Table 2). Deletion of chromosome 6q was demonstrated in 26 patients (19%) with 6q15–21 involvements in 18 of them. The chromosomal abnormality t(14;18) (q32;q21) was found in 17 of 28 patients (61%) with follicular center cell lymphoma, follicular type (FCC). It frequently accompanied with deletion of chromosome 6q (five cases, 29%). Seven patients were diagnosed as having Burkitt’s lymphoma; six of them had t(8;14) (q24;q32) and the remaining patient, both t(8;22) (q24;q11) and t(14;18) (q32;q21). Four of the five patients with mantle-cell lymphoma had t(11;14) (q13;q32). Six patients showed t(3;14)

Table 1. Distribution of various subtypes of non-Hodgkin’s lymphoma according to the REAL classification

<table>
<thead>
<tr>
<th>B cell</th>
<th>No. of patients</th>
<th>T cell</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicular</td>
<td>28 (14%)</td>
<td>Lymphoblastic</td>
<td>10 (5%)</td>
</tr>
<tr>
<td>Diffuse large B cell</td>
<td>77 (38.5%)</td>
<td>ALCL</td>
<td>9 (4.5%)</td>
</tr>
<tr>
<td>Mantle cell</td>
<td>5 (2.5%)</td>
<td>Angiocentric T/NK cell</td>
<td>11 (5.5%)</td>
</tr>
<tr>
<td>Burkitt’s lymphoma</td>
<td>7 (3.5%)</td>
<td>ATLL</td>
<td>9 (4.5%)</td>
</tr>
<tr>
<td>Small lymphocytic</td>
<td>7 (3.5%)</td>
<td>Hepatosplenic T-g/d</td>
<td>3 (1.5%)</td>
</tr>
<tr>
<td>Lymphoplasmacytoid</td>
<td>5 (2.5%)</td>
<td>PTCL</td>
<td>17 (9.5%)</td>
</tr>
<tr>
<td>Marginal zone</td>
<td>2 (1%)</td>
<td>AILD</td>
<td>2 (1.0%)</td>
</tr>
<tr>
<td>Others</td>
<td>7 (3.5%)</td>
<td>Unclassified</td>
<td>1 (0.5%)</td>
</tr>
<tr>
<td>Total</td>
<td>138 (69%)</td>
<td>Total</td>
<td>62 (31%)</td>
</tr>
</tbody>
</table>

*Per cent of total non-Hodgkin’s lymphoma.
AILD, angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large-cell lymphoma; ATLL, adult T-cell lymphoma/leukemia; PTCL, peripheral T-cell lymphoma, unspecified; REAL, Revised European–American Lymphoma; T/NK, angiocentric T/natural killer cell lymphoma.
(q27;q32) or t(3;22) (q27;q11); five of them had diffuse large B-cell lymphoma.

The median overall survival in the patients with B-cell lymphoma was 21 months (range 1–183 months). The prognostic implication of the three recurrent chromosomal aberrations including trisomy 12, trisomy 3 and deletion of 6q was analyzed. The patients with trisomy 12 showed a trend of shorter overall survival than those without (18 months versus 24 months, \( P = 0.08 \)). There was no difference in the overall survival between the patients with or without deletion of chromosome 6q (21 months versus 24 months, \( P = 0.51 \)), and between those with or without trisomy 3 (39 months versus 21 months, \( P = 0.31 \)).

Cytogenetic results of T-cell NHL and their correlation with histopathological subtypes and clinical outcomes

Sixty-two patients (31%) were diagnosed as having T-cell lymphoma. The distribution of the histopathological subtypes is shown in Table 1. Eleven patients had nasal (six patients) or nasal-type (five patients) angiocentric T/NK-cell lymphoma, nine had adult T-cell lymphoma/leukemia (ATLL) and only two had angioimmunoblastic T-cell lymphoma (AILD). Fifty patients (81%) had clonal chromosomal abnormalities; 27 of them showed complex changes with more than four abnormalities. The modal chromosome number ranged from 40 to 96, most commonly pseudodiploidy (20 patients) and hyperdiploidy between 47 and 50 (12 patients). The distribution of chromosome gain and loss among the 44 patients with near- or pseudodiploid chromosomes is shown in Figure 1. The most common recurrent numerical aberrations were monosomy 17 (16%), −Y (14%), trisomy 8 (11%), trisomy 7 (9%), −6 (9%), −X (9%) and monosomy 13 (7%). Trisomy 3 and 5 were demonstrated in only two and one case, respectively. The distribution of the structural chromosomal abnormalities among the 50 patients with clonal abnormalities is shown in Figure 2. Deletion of the chromosome 6q was found in 15 patients (30%, Table 3), most commonly involving 6q21–25 (12 patients). Other structural aberrations included 11q deletion (20%), 17p deletion (16%), 1q duplication (14%), 1p deletion (14%), 4q deletion (10%), 9q deletion (10%) and 6p duplication (8%) (Table 3). Duplication of 8q was found in three patients and deletion of 13q in none.

The non-random cytogenetic aberrations of T-cell lymphoma and their correlation with subtypes are shown in Table 3. The t(2;5) was detected in one of the nine patients with anaplastic large-cell lymphoma. Isochromosome of 7q, i(7) (q10) was demonstrated in all three patients with hepatosplenic T-γ6 lymphoma, but was also present in other subtypes of T-cell lymphoma. Chromosomal abnormalities involving 14q11 and 7q34–36, where T-cell receptor genes are located, were only found in four and one patient, respectively.

![Figure 1](https://example.com/figure1.png)

**Table 1.** Distribution of chromosome gain (●) and loss (□) in the 44 T-cell lymphoma patients with near- or pseudodiploid chromosomes.
All 11 patients with angiocentric nasal or nasal-type T/NK-cell lymphoma had clonal chromosomal aberrations. Six had complex changes with more than four abnormalities and two, three abnormalities. The non-random abnormalities included isochromosome of 7q (two patients), duplication of 1q (five patients, two with isochromosome of 1q and three with unbalanced translocation of duplicated segment distal to 1q21 to other chromosomes), deletion of 6q (four patients), and deletion of 11q23 (five patients, with 11q23–25 involvement in four of them). Three patients, all having nasal lesions, showed duplication of 6p; two presented as i(6)(p10) and one, der(6)t(6;6)(q23;p11). Compared with other subtypes of T-cell lymphoma, the patients with angiocentric T/NK-cell lymphoma had a significantly higher frequency of 1q duplication (45% versus 4%, \(P=0.001\)), 6p duplication (27% versus 2%, \(P<0.001\)) and 11q deletion (45% versus 10%, \(P=0.011\)) than others (Table 3). Nine patients had adult T-cell leukemia/lymphoma (ATLL) and positive serologic tests for human T-cell leukemia virus type I (HTLV-1). Five patients had complex chromosomal changes with more than four abnormalities and two patients, three abnormalities. There were no specific aberrations.

The median overall survival in the patients with T-cell lymphoma was 10 months (range 1–172 months). There was no prognostic implication of the most common recurrent chromosomal aberrations, including deletion of 6q, 17p deletion/monosomy 17, deletion of 11q, duplication of 1q and deletion of 1p.

Discussion

In this study, a total of 138 patients (69%) were diagnosed as having B-cell lymphoma. The incidence of follicular lymphoma among all NHL was lower in this area (14%) than in North America, London and Capetown (~30%) [3], but was similar to that in Asian countries (~10%) [3, 4, 12]. On the other hand, the distribution of diffuse large B-cell lymphoma was not much different among various geographical areas (38.5% in Taiwan versus 28–29% in North America, 28% in Capetown, 27–36% in Europe and 36% in Hong Kong) [3]. The same was also true for Burkitt’s lymphoma (3.5% in this study compared with 2–5% in most other areas) [4, 9, 19].

Table 3. Correlation of the recurrent chromosomal abnormalities with subtypes of T-cell lymphoma

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>T-LBL</th>
<th>ALCL</th>
<th>T/NK</th>
<th>ATLL</th>
<th>T-(\gamma)/d</th>
<th>PTCL</th>
<th>Others</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>t(2;5) (9p23;q35)</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>7q34–36</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>14q11</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>i(7) (q10)</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>1p deletion</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>1q duplication</td>
<td>1</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>6p duplication</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>6q deletion</td>
<td>0</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>Trisomy 7</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>11q deletion</td>
<td>1</td>
<td>0</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Monosomy17</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>17p deletion</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>8</td>
</tr>
</tbody>
</table>

T-LBL, T-lymphoblastic lymphoma; ALCL, anaplastic large-cell lymphoma; T/NK, angiocentric T/natural killer cell lymphoma; ATLL, adult T-cell lymphoma/leukemia; T-\(\gamma\)/d, hepatosplenic T-\(\gamma\)/d cell lymphoma; PTCL, peripheral T-cell lymphoma, unspecified; others, including AILD and unclassified T-cell lymphoma.
Reflecting the geographical difference in the distribution of follicular lymphoma, the frequency of t(14;18) among total NHL was lower in this area (24 patients, 12%, Table 2) than in the USA (~30%) and Europe (~20%) [9, 19], but was comparable to that in Japan [12]. However, the incidence of t(14;18) in follicular lymphoma in Taiwan (17 of 28 patients, 61%) was similar to that in the West (50–60%) [9, 19]. It is suggested that though some environmental or genetic factors may influence the prevalence of follicular lymphoma in different areas, the pathogenesis of this subtype of NHL is similar worldwide. The 8q24 abnormalities, including t(8;14), t(2;8), t(8;22) and other rearrangements involving 8q24, showed even geographical distribution (6% in this study, 10% in the USA, 10% in Europe and 6% in Japan) [19]. The finding that all patients with Burkitt’s lymphoma showed either t(8;14) or t(8;22) (Table 2) confirmed the close association of the chromosomal translocations with this subtype of lymphoma [20].

In this study, 62 patients (31%) had T-cell lymphoma, an incidence similar to those reported previously in Asia [4], but much higher than in western countries (~10%) [21]. The frequency of AILD in T-cell lymphoma was lower and that of ATLL and angiocentric T/NK-cell lymphoma was higher in this area (Table 1) than in the West [21]. It is not easy to compare the chromosomal abnormalities of T-cell lymphoma among different geographical areas because the reports are few and various histological classifications were used [13, 14, 22]. In this study, the patients with T-cell lymphoma had low incidences of trisomy 3 and trisomy 5 [two patients (4%) and one patient (2%), respectively], compared with those in the West (16–32% and ~15%, respectively) [13, 14, 23]. These two numerical abnormalities are closely correlated with AILD [13], a subtype of T-cell lymphoma very common in western countries [14, 21], but rare in Taiwan. Trisomy 3 has also been detected frequently in ATLL patients in endemic areas; however, only one of the nine patients with ATLL in this area, a non-endemic area, showed this change. None of the three NHL patients with antibody to ATLL-associated antigen in Saitama, a non-endemic area, had trisomy 3, either [24].

On the other hand, 10 patients (16%) with T-cell lymphoma in this study had deletion of 11q, which was an uncommon structural aberration of T-cell lymphoma in previous reports [13, 23]. This chromosomal aberration is also rare in B-cell lymphoma other than small lymphocytic lymphoma [25]. It was only found in seven (5%) of 138 patients with B-cell lymphoma in this study (data not shown). Interestingly, patients with angiocentric T/NK-cell lymphoma had a significantly higher incidence of 11q deletion than other subtypes of T-cell lymphoma (Table 3). Most patients with this subtype of lymphoma and deletion of 11q involved 11q23–25. If the finding is confirmed by further studies on a large number of patients, search for a suppressor gene in 11q23–25 may be helpful for understanding the pathogenesis of angiocentric T/NK-cell lymphoma.

Duplication of 6p was found to be associated with mycosis fungoides and Sezary syndrome [13, 23], but was uncommon in other subtypes of lymphoma [9, 13, 20]. In this study, 6p duplication was highly correlated with nasal angiocentric T/NK-cell lymphoma. Three of the six patients with this subtype of lymphoma showed 6p duplication; two presented as i(6) (p10) and one of them as the sole aberration [15]. For comparison, only one patient (2%) with other T-cell lymphoma and five patients (4%) with B-cell lymphoma (data not shown) had this change. Although the patients with T-cell lymphoma in this study had a high incidence of monosomy 17 and deletion of 17p, which was not shown in previous reports, the abnormalities did not show subtype propensity.

In summary, the incidence of follicular lymphoma is lower and T-cell lymphoma is higher in Taiwan than in the West, and among T-cell lymphoma there are fewer AILD but more angiocentric T/NK-cell lymphoma in Taiwan. Although the frequency of t(14;18) among total NHL is low in Taiwan, the occurrence of the aberration among follicular lymphoma here is similar to that in the West. In T-cell lymphoma, the incidences of trisomy 3 and trisomy 5, two common abnormalities in AILD, are quite low, but deletion of 11q, a chromosomal change significantly more frequent in angiocentric T/NK-cell lymphoma than other T-cell NHL, is high in this area, compared with western countries. These findings suggest that the geographical differences in the chromosomal aberrations of NHL reflect the differences in the distribution of histological subtypes of lymphoma among various areas. The pathogenesis of each subtype of lymphoma may be similar worldwide.

References