Leukaemia Section
Review

+X solely in lymphomas
Adriana Zamecnikova
Kuwait Cancer Control Center, Department of Hematology, Laboratory of Cancer Genetics, Kuwait; annaadria@yahoo.com

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Abstract
Review on +X solely in lymphomas, with data on clinics.

KEYWORDS
X chromosome gain, malignant lymphoma, chronic lymphocytic leukemia, gene downregulation.

Clinics and pathology
Disease
B- and T-cell lymphomas and chronic lymphocytic leukemia (CLL).

Phenotype/cell stem origin
39 lymphoma cases to date; among them, lymphomas with B-cell phenotype in 26 patients: follicular lymphoma (FL, n=6) (Rosenwald et al 1999; Horsman et al 2001; Goodlad et al 2003; Fan & Rizkalla 2003; Rajgopal et al 2003; Aamot et al 2007), diffuse large B-cell lymphomas (DLBCL, n=6) (Koduru et al., 1987; Konishi et al., 1990; Cigudosa et al., 1999; Cerretini et al., 2006; Niitsu et al., 2009; Niitsu et al., 2009); mature B-cell neoplasm (n=3, MBCN) (Maseki et al., 1987; Coignet et al., 1996; Cook et al., 2004), nodal marginal zone B-cell lymphoma (NMZL, n=3) (Cook et al., 2004; Aamot et al., 2005; Martin-Subero et al., 2007); splenic marginal zone B-cell lymphoma (SMZL, n=3) (Dierlamm et al., 1996; Le Baccon et al., 2001; Narayan et al., 2013), Hodgkin disease (HD, n=3) (Dennis et al., 1989; Schlegelberger et al., 1994; Falzetti et al., 1999), 1 post-transplant lymphoproliferative disorder with primary non-Hodgkin lymphoma (Djokic et al., 2006) and 1 mantle cell lymphoma case (Siebert et al., 1998). Various T-cell malignancies in 13 patients: most often angioimmunoblastic T-cell lymphoma (ATCL, n=6) (Godde-Salz et al., 1987; Kaneko et al., 1988; Schlegelberger et al., 1990), mature T- and NK-cell neoplasm (n=2) (Hashimoto et al., 1995), mycosis fungoides/Sezary syndrome (n=2) (van Vloten et al., 1979; Limon et al., 1995), adult T-cell lymphoma/leukemia (HTLV-1+) (ATL, n=2) (Sanada et al., 1986; Itoyama et al., 2001) and 1 there was 1 unspecified peripheral T-cell lymphoma case (Schlegelberger et al., 1994) (Table 1).

<table>
<thead>
<tr>
<th>Sex/Age</th>
<th>Disease</th>
<th>Karyotype</th>
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Atlas Genet Cytogenet Oncol Haematol. 2018; 22(9)
### Mycotics fungoides/Sezary syndrome

**F/755**

46,XX,del(3)(p11),+8,add(10)(q13),+mar/47,XX,+X

### Adult T-cell lymphoma/leukemia (HTLV-1+)

**F/62**

46,XX,add(2)(p13),del(3)(q21q27)/45,X,-X/47,XX,+X

### Angioimmunoblastic T-cell lymphoma

**M/75**

47,XY,+X/47,idem,del(10)(p12) LN

**F/64**

47,XX,+X LN

### Diffuse large B-cell lymphoma

**F/73**

47,XX,+X LN

### Mature B-cell neoplasm, NOS

**M/82**

47,XY,+X LN

### Angioimmunoblastic T-cell lymphoma

**F/63**

47,XX,+add(3)(p11)/47,XX,+X LN

### Hodgkin disease, NOS

**M/49**

47,XY,+X LN

### Diffuse large B-cell lymphoma

**M/72**

47,XY,+X LN

### Angioimmunoblastic T-cell lymphoma

**F/63**

49,XX,+5,+19,+21/47,XX,+X/46,XX,inv(14)(q11q32)/45,X,-X LN

### Angioimmunoblastic T-cell lymphoma

**F/78**

47,XX,+X LN

### Angioimmunoblastic T-cell lymphoma

**F/47**

47,XX,+X LN

### Hodgkin disease, nodular sclerosis

**F/35**

78-82,XX,-X,-X,(1)(q10),add(5)(p?),del(6)(q?)x2,add(7)(q?),del(9)(p?),hsr(11)(p?),add(19)(q?),+mar/47,XX,+X LN

### Peripheral T-cell lymphoma, unspecified

**F/65**

47,XX,+X

### Mature T- and NK-cell neoplasm, NOS

**M/54**

47,XY,+X/35-42,XY,der(1;13)(q10;q10),der(1;14)(p10;q10) LN

### Mature T- and NK-cell neoplasm, NOS

**M/78**

47,XY,+X LN

### Mycosis fungoides/Sezary syndrome

**F/64**

43-45,XX,del(3)(p11),i(6)(p10),+8,add(10)(q24),del(12)(p11),der(17)t(3;17)(q12;p11),add(19)(q13),+mar,inc/47,XX,+X/41-44,XX,+7,inc

### Mature B-cell neoplasm, NOS

**F/89**

47,XX,+12/47,XX,+X LN

### Splenic marginal zone B-cell lymphoma

**F/57**

47,XX,+X LN

### Mantle cell lymphoma

**F/60**

80-88,XXXX,+X,add(1)(q32),del(1)(q24),-4,-6,del(6)(q21q23),-9,t(11;14)(q32;q32),add(12)(q24),-13,-13,der(14)t(11;14),-15,-15,+16,-19,-22,+3mar/47,XX,+X LN
<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Diagnosis</th>
<th>Karyotype</th>
<th>Reference</th>
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</thead>
<tbody>
<tr>
<td>21</td>
<td>F</td>
<td>Diffuse large B-cell lymphoma</td>
<td>47,XX,+X LN</td>
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</tr>
<tr>
<td>22</td>
<td>F/16</td>
<td>Hodgkin disease, nodular sclerosis</td>
<td>47,XX,+X LN</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>F</td>
<td>Follicular lymphoma</td>
<td>47,XX,+X LN</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>F/73</td>
<td>Splenic marginal zone B-cell lymphoma</td>
<td>46,XX,del(p1)(q21),del(7)(q23q36)/47,XX,+X LN</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>F/32</td>
<td>Adult T-cell lymphoma/leukemia (HTLV-1+)</td>
<td>47,XX,+X/49,XX,+del(3)(p13),+5,+11</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>M/51</td>
<td>Follicular lymphoma</td>
<td>47,XY,+X/49,idem,t(14;18)(q32;q21),+18,+21</td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>F/62</td>
<td>Follicular lymphoma</td>
<td>51,XX,+X,del(4)(q31),add(10)(p13),t(14;18)(q32;q21),+18,+21,+14;21,del(7)(q11),+mar</td>
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<tr>
<td>28</td>
<td>M</td>
<td>Follicular lymphoma</td>
<td>47,XY,+X/47-49,idem,+7,t(9;10)(p10;q10),t(14;18)(q32;q21),+21</td>
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</tr>
<tr>
<td>29</td>
<td>M/51</td>
<td>Follicular lymphoma</td>
<td>47,XX,+X/49-52,XY,+X,del(14;18)(q32;q21),+21,+mar</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>F</td>
<td>Nodal marginal zone B-cell lymphoma</td>
<td>48,XX,+3,de(11)(q23),del(13)(q12q14),+18/47,XX,+X LN</td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>M</td>
<td>Mature B-cell neoplasm, NOS</td>
<td>47,XY,+X/50,idem,+X,add(1)(p36),trp(1)(q21q32),+add(2)(p23),+der(3;4)(p10;q10),add(6)(p25),+12,der(14;15)(p10;q10)add(22)(p11),+mar</td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>F/75</td>
<td>Nodal marginal zone B-cell lymphoma</td>
<td>47,XX,+X LN</td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>M/36</td>
<td>Diffuse large B-cell lymphoma</td>
<td>47,XY,+X</td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>F/40</td>
<td>Post-transplant lymphoproliferative disorder</td>
<td>47,XY,+X primary non-Hodgkin lymphoma</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>M</td>
<td>Follicular lymphoma</td>
<td>47,XY,+X/47,idem,der(1)add(1)(p36)t(1;6)(q32;q13),del(6)t(1;6),del(13)(q31),t(14;18)(q32;q21) LN</td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>F/85</td>
<td>Nodal marginal zone B-cell lymphoma</td>
<td>46,XX,del(1)(q24-43),der(7)(t3)(q21)(q34-35)/48,del(6)t(14;18)(q23-24),der(3)ins(3;7)(q24;?),+der(3)t(3;7)(p25;?),t(14;19)(q32;q13),+mar/47,XX,+X LN</td>
<td></td>
</tr>
<tr>
<td>37</td>
<td>M/54</td>
<td>Diffuse large B-cell lymphoma</td>
<td>55,XY,+X,del(3)(t8;14)(q32),t(14;18)(q32;q21)/47,XY,+X LN</td>
<td></td>
</tr>
<tr>
<td>38</td>
<td>F/44</td>
<td>Diffuse large B-cell lymphoma</td>
<td>47,XX,+X,del(3)(t8;14)(q32),t(14;18)(q32;q21)/47,XY,+X LN</td>
<td></td>
</tr>
<tr>
<td>39</td>
<td>M/50</td>
<td>Splenic marginal zone B-cell lymphoma</td>
<td>47,XY,+X LN</td>
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</tr>
</tbody>
</table>

Abbreviations: M, male; F, female; LN, lymph node.
Chronic lymphocytic leukemia was found in 16 patients (Barbieri et al., 1984; Ohtaki et al., 1986; Asou et al., 1994; Arif et al., 1995; Mould et al., 1996; Geisler et al., 1997; Lopez et al., 2012) (Table 2).

<table>
<thead>
<tr>
<th>Sex/Age</th>
<th>Karyotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 F/40</td>
<td>47,XX,+X</td>
</tr>
<tr>
<td>2 F/59</td>
<td>47,XX,+12/47,XX,+8/47,XX,+16/47,XX,+17/47,XX,+18/47,XX,+X/46,XX,del(6)(q)?/46,XX,del(10)(q)?</td>
</tr>
<tr>
<td>3 F</td>
<td>47,XX,+X</td>
</tr>
<tr>
<td>4 F/79</td>
<td>47,XX,+X/46,XX,-1,+15</td>
</tr>
<tr>
<td>5 F</td>
<td>47,XX,+12/47,idem,del(13)(q12q14)/47,XX,+X</td>
</tr>
<tr>
<td>6 F</td>
<td>47,XX,+X</td>
</tr>
<tr>
<td>7 F</td>
<td>47,XX,+X</td>
</tr>
<tr>
<td>8 F</td>
<td>45,X,-X/47,XX,+X</td>
</tr>
<tr>
<td>9 F</td>
<td>46,XX,del(6)(q15q22)/47,XX,+X</td>
</tr>
<tr>
<td>10 F</td>
<td>47,XX,+X</td>
</tr>
<tr>
<td>11 M</td>
<td>47,XY,+X</td>
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</tbody>
</table>

Clinical and karyotyping data in chronic lymphocytic leukemia patients.

**Epidemiology**

14 males and 25 females with various forms of lymphomas (aged 16 to 89 years; median age 62 years); median age was 62 years in B-cell lymphomas (11 males and 15 females aged 16 to 89 years); female prevalence in T-cell malignancies (3 males, 10 females aged 32 to 78 years). Similarly, there is a female prevalence in chronic lymphocytic leukemia patients (3 males and 13 females), aged 40 to 79 years (from the known data).

**Prognosis**

Unknown, due to the heterogeneity of diseases; (indolent versus aggressive disease); patients with only numerical abnormalities may have better outcome than patients with structural changes in a sideline.

**Cytogenetics**

Out of 39 lymphoma patients, the extra chromosome X was found in a sideline in 22 cases: Found in association with t(8;14)(q24;q32) and t(14;18)(q32;q21) in 1 DLCL (Niitsu et al., 2009), t(14;18)(q32;q21) in 5 FL (Horsman et al., 2001; Goodlad et al., 2003; Fan and Rizkalla, 2003; Rajgopal et al., 2003; Aamot et al., 2007), t(11;14)(q13q32) in 1 MCL (Siebert et al., 1998), del(11)(q23) and del(13)(q12q14) in 1 NMZL (Cook et al., 2004), t(14;19)(q32;q13) in 1 NMZL (Martin-Subero et al., 2007), t(11;14)(q13q32) in 1 MCL (Siebert et al., 1998) and miscellaneous anomalies in 4 B-cell lymphomas (Schlegelberger et al., 1994; Coignet et al., 1996; Le Baccon et al., 2001; Cook et al., 2004). Associated withinv(14)(q11q32) in 1 patient with angioimmunoblastic T-cell lymphoma (Schlegelberger et al., 1990) and miscellaneous anomalies in 7 patients with T-cell lymphomas (van Vloten et al., 1979; Sanada et al 1986; Godde-Salz et al., 1987; Kaneko et al., 1988; Hashimoto et al., 1995; Limon et al 1995; Itoyama et al 2001). Found in a sideline in 7 out of 16 CLL patients. Among them: in association with +12 in 3 (Ohtaki et al., 1986; Mould et al., 1996; Lopez et al., 2012), -X in 1 (Geisler et al., 1997), del(6)(q15q22) in 1 (Geisler et al., 1997), der(8;17)(q10;q10) in 1 (Geisler et al., 1997); and -1, +15 in 1 (Arif et al., 1995).
Whole chromosome gain of an X chromosome has been described in various types of hematological malignancies, including malignant lymphomas. Additional sex chromosomes are usually part of complex karyotypes, representing secondary karyotypic alterations in a significant proportion of lymphomas, and less frequently in CLL. While extra X chromosome is a known numerical abnormality in these diseases, its gain as the sole acquired abnormality is not a common feature. Numerical X chromosome changes are often found in a sideline, indicative of a multistep pathogenesis, where X chromosome gain would likely represent a relatively early genetic event. However, it is unclear whether +X alone is capable of promoting oncogenesis or aberrant effects of the trisomy might allow direct acquisition of cancer-promoting mutations.

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+X solely in lymphomas


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