Leukaemia Section
Short Communication


der(12)t(1;12)(q11-21;p11-13)

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Abstract

Review on t(1;12)(q11-21;p11-13), with data on clinics.

Clinics and pathology

Disease
Myeloid disorders, less frequently multiple myeloma and lymphoid malignancies

Note
The balanced t(1;12)(q21;p13) translocation results in a ETV6 / ARNT fusion gene.

Phenotype/cell stem origin
16 cases with an unbalanced sex ratio (11 males/5 females aged 0 to 79-years old). Most cases were diagnosed with myeloid malignancies (10 patients; 7 males and 3 females aged 0 to 72 years old): 3 patients with refractory anemia (RA) (Pedersen-Bjergaard et al., 1998; Andersen et al., 2005; Gerr et al., 2006), among them 2 were treated for multiple myeloma (MM) (Pedersen-Bjergaard et al., 1998; Andersen et al., 2005) and 7 patients were diagnosed with acute myeloid leukemia (AML) (Trent et al., 1983; La Starza et al., 1999; Odero et al., 2001; Andersen et al., 2005; Fitzgibbon et al., 2005; Raghavan et al., 2005; Gerr et al., 2006; Tuborgh et al., 2013; Parihar et al., 2014).

The AML cases were most often M5 AML (5/7) and in this small AML M5 series, 3 cases are found in infant patients. 3 cases were diagnosed with multiple myeloma (Calasanz et al., 1997; Gonzalez et al., 2004; Gabrea et al., 2008) and 3 with lymphoid malignancies: chronic lymphocytic leukemia (CLL) (Miymoto et al., 1981), Burkitt’s lymphoma (Schoch et al., 1995) and mature B-cell neoplasm (Kuroda et al., 2000) (Table 1).

Prognosis
Unknown; may be unfavorable in association with complex karyotypes and in association with poor-risk genetic features.

Cytogenetics

Cytogenetics morphological
Unbalanced rearrangement; breakpoint has been defined on 1q to be between q11-q21; breakpoints in 12p are heterogeneous (assigned to chromosome bands from 12p11 to p13); most of cases reported 12p13 breakpoint (9 out of 16 cases). Sole aberration in 3 AML patients (Trent et al., 1983; Fitzgibbon et al., 2005; Raghavan et al., 2005) and part of a complex karyotype in the remaining AML cases that are associated with +8 in 3 (La Starza et al., 1999; Gerr et al., 2006; Tuborgh et al., 2013) and 11q23 aberration in 2 patients (Odero et al., 2001; Tuborgh et al., 2013). Found in complex karyotypes and in association with t(11;14)(q13;q32) in 1 MM patient (Calasanz et al., 1997) and with 8q24 rearrangement in both lymphoma cases (Schoch et al., 1995; Kuroda et al., 2000).
<table>
<thead>
<tr>
<th>Sex/Age</th>
<th>Disease</th>
<th>Karyotype</th>
<th>Ref.</th>
</tr>
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<tbody>
<tr>
<td>M/72</td>
<td>AML</td>
<td>46,XY,der(12)t(1;12)(q21;p13)</td>
<td>1</td>
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<tr>
<td>F/59</td>
<td>RA, post-MM</td>
<td>43,X,-X,t(3;21)(q26;q22),del(4)(p14p16),-6,-8,del(10)(p11),der(12)(t(1;12)(q21;p12),-13,-14,del(20)(p12),add(22)(q12),+3mar</td>
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<tr>
<td>M/55</td>
<td>AML-M6</td>
<td>48,XY,+8,der(12)(t(1;12)(q21;p13),+mar/48,idem,add(7)(q2)</td>
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<tr>
<td>F/1</td>
<td>AML-M5</td>
<td>46,XX,t(9;11)(p22;q23),del(17)(p13),der(22)(t(17;22)(p13;q13)/47,XX,+der(9)</td>
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<tr>
<td>M/66</td>
<td>RAEBI, post-MM</td>
<td>45,47,XY,+del(1)(p21),dic(1;7)(p11;q11),der(6)(t(3;6)(p22;q22),dic(7;13)(p11;p11),der(12)(t(1;12)(q21;p13)</td>
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<td>AML-M5</td>
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<td>AML-M5</td>
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<td>M/63</td>
<td>RAEBI</td>
<td>47,XY,+add(9)(p11),+add(9)(q11),del(20)(p11),+21,add(21)(p11)x2/47,der(1)(p34)(t(1;21)(q12;p12),der(12)(t(1;12)(q12;p12),add(14)(p11),-add(21)</td>
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<td>M/0</td>
<td>AML-M5</td>
<td>47,XY,t(6;19;11)(p22;p13;q23),+der(6)(t(6;11)(p22;p23)/48,iderm,8/48,iderm, +8,der(12)(t(1;12)(q11;p13)/48.X,der(Y)(t(Y;1)(q12;q11),t(6;19;11),+der(6)(t(6;11)</td>
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<tr>
<td>F/1</td>
<td>AML-M5</td>
<td>46,XX,der(12)(t(1;12)(q12;p13)/46,XX,der(13)(t(1;13)(q12;p12)</td>
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<td>M</td>
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<tr>
<td>M</td>
<td>Multiple myeloma</td>
<td>45,XY,der(12)(t(1;12)(q21;p13),-13</td>
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<tr>
<td>F</td>
<td>Multiple myeloma</td>
<td>46-47.X,-X,der(1;16)(q10;p10),-4,+5,+7,t(8;22)(q24;q11),der(12)(t(1;12)(q11-12:p13),-13,+del(15)(q12q13),der(17)(t(17;17)(q11-12;p13),+18,der(20)(t(19;20)</td>
<td>13</td>
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<td>B-cell neoplasms</td>
<td>M46</td>
<td>CLL</td>
<td>??,XY,del(1)(q2?),t(1;10)(q11;p1?5),der(12)(t(1;12)(q11;p12)</td>
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<td>M/40</td>
<td>BL</td>
<td>46,XY,t(8;14)(q24;q32),der(12)(t(1;12)(q21;p13),add(14)(q32/46,der(17)(t(17;17)(p11;11),add(18)(p11)</td>
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<td>B-cell neoplasm</td>
<td>48,XX,t(8;22)(q24;q11),der(12)(t(1;12)(q21;p13),+17,mar</td>
<td>16</td>
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</tbody>
</table>


### Genes involved and proteins

This unbalanced translocation is likely to be molecularly heterogeneous and whether the same gene(s) are involved in both myeloid and lymphoid malignancies is unknown.

### Result of the chromosomal anomaly

**Fusion protein**

**Oncogenesis**

Unbalanced translocations between the long arm of chromosome 1 and the short arm of chromosome 12 are infrequent but might be relatively specific to myeloid-lineage malignancies. Although cytogenetically heterogeneous, der(12)(t(1;12)(q11-21;p11-13) results in a gain of 1q leading to genomic imbalances. Gains/amplification of 1q are common in a broad spectrum of myeloid and lymphoid haematological malignancies indicating that that genes of the 1q region may provide selective growth
advantages for the leukemic cells in a variety of neoplasms.

The unbalanced der(12)t(1;12)(q11-21;p11-13) may be present as the sole anomaly or in association with complex karyotypes, implicating that it may have a key role in disease initiation and/or progression. Alternatively, it is possible that genes on the 12p11-p13 region may also be involved in disease pathogenesis either as a result of the chromosome translocation and/or deletions. Notably, chromosome 12 breakpoint in der(12)t(1;12)(q11-21;p11-13) is most often localized on 12p13, that include the TEL/ETV6 gene, therefore it is possible that ETV6 may be affected by the translocation, at least in some patients. In addition, 12p rearrangements are frequently accompanied by small interstitial deletions that include ETV6 and CDKN1B among other genes. Thus, haploinsufficiency or loss of tumor suppressor function of genes located on the 12p11-p13 region may play a role in oncogenesis. Whether genes located on the 12p11-p13 region are involved in this aberration has not been determined.

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