Abstract

Complete or partial monosomies of the long arm of chromosome 5 and/or 17p are common findings in myeloid malignancies, particularly in therapy-related myeloid disorders. They usually result from interstitial or terminal deletions and less frequently from unbalanced rearrangements such as dicentric chromosomes. One of the recurring unbalanced translocation in myeloid malignancies is the unbalanced dicentric translocation dic(5;17)(q11-14;p11-13) that results in complete or partial monosomy for the long arm of chromosome 5 and the short arm of chromosome 17.

Keywords
dicentric; chromosome 5; chromosome 17; chronic myelogenous leukemia; acute myeloid leukemia; myelodysplastic syndrome; therapy-related leukemia.

Identity

Note
Included are 5q11-14 and 17p11-13 breakpoints (breakpoints described at or near the centromeres), the related unbalanced der(5)t(5:17) and der(17)t(5:17) are not included.

Figure 1
**Clinics and pathology**

**Disease**

Chronic myeloproliferative neoplasms and acute myeloid leukemia (AML)

16 patients had a primary myelodysplastic syndrome (MDS) (Knapp et al., 1985; Herry et al., 2007; Lang et al., 2010) or de novo AML (Huret et al., 1991; Kwong et al., 1994; Arkesteijn et al., 1996; Tosi et al. 1996; Wang et al., 1997; Mrozek et al., 2002; Zatkova et al., 2006; Herry et al., 2007; Hangai et al., 2013) and 2 patients had chronic myelogenous leukemia in advanced phase (Hagemeijer et al., 1981; Wang et al., 1997). 23 patients developed therapy-related MDS (Hatzis et al., 1995; Wang et al., 1997; Andersen et al., 2005; Andersen et al., 2008) or AML (Kerim et al., 1991; Heyne et al., 1994; Wang et al., 1997; Nakamori et al., 2003; Andersen et al., 2005; McNerney et al., 2014) after cytotoxic treatment and/or radiotherapy (Table 1).

<table>
<thead>
<tr>
<th>Sex/Age</th>
<th>Diagnosis</th>
<th>Karyotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CML</td>
<td>44-45,XY, dic(5;17)(q11:p11), t(9;22), r(18) blast crisis</td>
</tr>
<tr>
<td>2</td>
<td>RAEB</td>
<td>45,XY, dic(5;17)(q11:p11), -7,+8/46, idem, add(18)(q23), +mar</td>
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<tr>
<td>3</td>
<td>AML-M2</td>
<td>45,XY, +8/46,XY, -5, -17, -18,+mar/44,XY,dic(5;17)(q11:p11), -18/46,XY,dic(5;17), -18,+mar idiopathic myelofibrosis, chemotherapy</td>
</tr>
<tr>
<td>4</td>
<td>AML-M1</td>
<td>45,XY, hsr(2)(q22), dic(5;17)(q11:p11), der(7)del(7)(q11)hslr(7)(q11), der(12)t(12;19)(p11;q12), -19, +mar embryonal rhabdomyosarcoma, chemotherapy, radiotherapy</td>
</tr>
<tr>
<td>5</td>
<td>M1</td>
<td>47,XY, +14/45,XY, dic(5;17)(q11:p11), dmin/95-96,XY, -Y, -5,+9,+11,+12,+13,+14,+14,+17</td>
</tr>
<tr>
<td>6</td>
<td>M77</td>
<td>47,XY, -d(5;17)(q11:p11) acute promyelocytic leukemia, relapse, chemotherapy</td>
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<tr>
<td>7</td>
<td>RAEB</td>
<td>45,XX, dic(5;17)(q11:p11)</td>
</tr>
<tr>
<td>8</td>
<td>AML-M1</td>
<td>46,XY, +7;5;15(p21;q23)(t;3;5)(q23;q12),ins(4;12)(q28;p?),dic(5;17)(q11:p11), der(7)(7;18)(q11;q12)(14;18)(q12;q23), +8,-14,del(18)(q12q23),add(19)(q23), +21</td>
</tr>
<tr>
<td>9</td>
<td>F63</td>
<td>46,XX, dic(5;17)(q11:p11), -7,der(10)t(10;19)(p11;q11), -19, +2mar</td>
</tr>
<tr>
<td>10</td>
<td>M75</td>
<td>46,XY, -d(5;17)(q11:p11), del(7)(q22?), +8,+11,-15,+mar</td>
</tr>
<tr>
<td>11</td>
<td>M66</td>
<td>43,XY, der(5)(t5;12)(q13;q14), dic(5;17)(q13;p11), -7, dup(9)(q21q12), -12,-15, add(16)(q13), add(17)(p11), -18, (+add(21)(p11), +mar/44, idem, +13</td>
</tr>
<tr>
<td>12</td>
<td>F64</td>
<td>45,XX, -d(5;17)(q13;p11), inv(5)(p13q11)/46,idem, +8/44, idem, -11,add(16)(p13), der(19)t(11;19)(q11q25)p13 add(11)(q11) multiple myeloma, chemotherapy</td>
</tr>
<tr>
<td>13</td>
<td>F50</td>
<td>45,XX, dic(5;17)(q13;p11), inv(5)(p13q11)/46,idem, +8/44, idem, -11,add(16)(p13)</td>
</tr>
<tr>
<td>14</td>
<td>F64</td>
<td>45,XX, add(1)(q42), add(4)(q225), dic(5;17)(q11:p11), der(6)t(6;12)(q21;q21), -12, -19, +mar/46, idem, +8/46, idem, +11, der(11;11)t(11;11)(p15;q25)ins(11;7)p15;q25, +46,idem, +11,der(11;11), +13, +mar</td>
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<tr>
<td>15</td>
<td>F73</td>
<td>43,XX, dic(3;22)(p21;p11), dic(5;17)(q11;p11), -7,+8,add(12)(p13),add(16)(p13), -11, add(16)(p13), der(19)t(11;19)(q11q25)p13 add(11)(q11) multiple myeloma, chemotherapy</td>
</tr>
<tr>
<td>16</td>
<td>F48</td>
<td>45,XX, add(1)(q42), add(4)(q225), dic(5;17)(q11:p11), der(6)t(6;12)(q21;q21), -12, -19, +mar/46, idem, +8/46, idem, +11, der(11;11)t(11;11)(p15;q25)ins(11;7)p15;q25, +46,idem, +11,der(11;11), +13, +mar</td>
</tr>
<tr>
<td>17</td>
<td>M55</td>
<td>44,XY, dic(5;17)(q13;p11), dic(19;20)(p13q11)/45,idem, +mar Hodgkin disease, chemotherapy</td>
</tr>
<tr>
<td>18</td>
<td>F81</td>
<td>47,XX, del(3)(p21p24), dic(5;17)(q13;p11), +8, +22, +28, +46, idem, +X adenocarcinoma, radiotherapy</td>
</tr>
<tr>
<td>19</td>
<td>M58</td>
<td>45,XY, dic(5;17)(q11;p11), t(7;7)(p22;q21?)hslr(7)(q11),hslr(7)(q11), hsr(7)(q11), der(13)(q12q14)/43,XY, dic(5;17), -7, dic(9;18)(q13p11)/44,XY,dic(5;17), -7, -16/46,XY,del(11)(q14q23) chronic lymphocytic leukemia, chemotherapy</td>
</tr>
</tbody>
</table>

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dic(5;17)(q11-p11)
dic(5;17)(q11-14;p11-13).
Zamecnikova A, al Bahar S

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Table 1. Reported patients with dic(5;17)(q11-14;p11-13).

Phenotype/cell stem origin
Phenotype / cell stem origin de novo and therapy related myeloid malignancies.

Epidemiology
29 male and 12 female patients (sex ratio 2.4) aged 1 to 86 years (median age 63 years).
There were 2 pediatric cases (aged 1 and 8 years), both of them developed AML after therapy for rhabdomyosarcoma.

Prognosis
Patients with 5q and/or 17p deletions and complex karyotypes represent an unfavorable cytogenetic prognostic category, particularly when the disorder is related to previous cytotoxic therapy.

Cytogenetics
Cytogenetics morphological
Presents as 1 normal chromosome 5 and 17 and a dic(5;17) chromosome that contains the short arm of chromosome 5, the long arm of chromosome 17 and centromeres of both chromosomes; breakpoints at or near the centromeres may be difficult to ascertain, the most common described breakpoints were q11 on chromosome 5 and p11 on 17p, reported in 31 out of 41 patients.
Combining karyotyping with fluorescence in situ hybridization of centromere-specific probes for chromosomes 5 and 17 allows precise breakpoint definition and confirm the presence of both centromeres.

Additional anomalies
Sole anomaly in 1 MDS patient previously treated for acute promyelocytic leukemia and found in association with increased karyotype complexity in most of the cases.
The most commonly observed anomaly was monosomy 7, observed in 19, while 7q deletion was found in 5 patients. Monosomy 5/5q- was found in 4 and +8 in 10 patients.

Result of the chromosomal anomaly

Fusion protein

Oncogenesis
Deletion of 5q and 17p through formation of an unbalanced dicentric rearrangement is a non-random event in myeloid malignancies, particularly in therapy-related disorders. dic(5;17)(q11-14;p11-13) result in partial monosomy for 5q and 17p leading to altered gene dosages, affecting tumor suppressor genes. The key mechanism might be the combined loss of tumor suppressor genes in 5q and 17p containing the TP53 gene. It is likely that TP53 loss that is frequently accompanied by inactivating mutations in the remaining TP53 allele (Wang et al., 1997) represent one of the instigators of the genome instability that is manifested by complex karyotypes. Highly complex rearrangements containing unbalanced translocations, ring chromosomes, insertions, marker chromosomes, homogeneously staining regions, dicentric chromosomes and cytogenetically unrelated clones were overrepresented in patients with therapy-related myeloid malignancies, indicative of the role of mutagenic effect of previous therapy. The probable sequence of genetic events is unclear; however dic(5;17) usually presents with additional common anomalies such as monosomy 7/7q or 5/5q and trisomy 8, therefore the formation of dic(5;17) likely represent a therapy-induced abnormality that occurred during the multistep process of leukemogenesis.

References
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