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Leukaemia Section
Short Communication

dic(5;17)(q11-14;p11-13)

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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 leukemmia.

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.

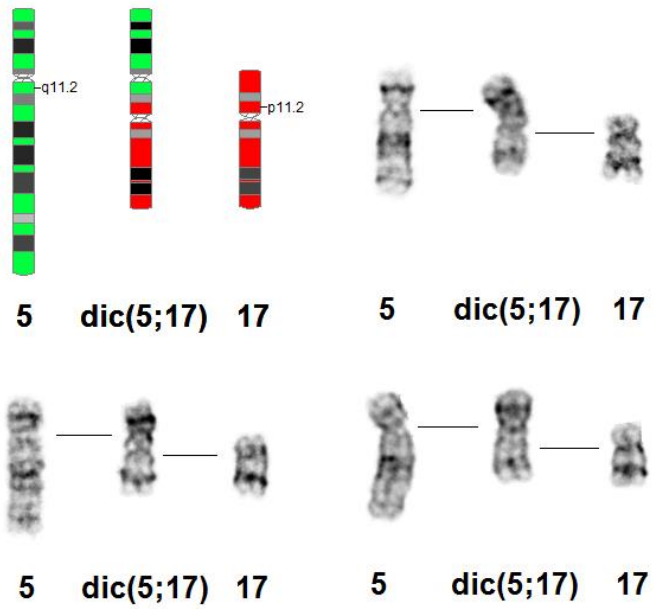

Figure 1 dic(5;17)(q11.2~13;p11.2~13) G- banding: - Courtesy Ronnie Ghuman and Charles D. Bangs.

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; Lange 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., Andersen et al., 2008) or AML (Kerim et al., 1991; Heyn 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).

	Sex/Age	Diagnosis	Karyotype
1	M/26	CML	44-45,XY,dic(5;17)(q11;p11),t(9;22),r(18) blast crisis
2	M/57	RAEB	45,XY,dic(5;17)(q11;p11),-7,+8/46,idem,add(18)(q23),+mar
3	M/69	AML-M2	45,XY,r(3),dic(5;17)(q14;p13),del(7)(q11),add(9)(p2?),add(9)(q34),-12,-13,i(21)(q10),+mar/90, idemx2
4	M/71	AML-M1	47,XY,+8/44,XY,-5,-17,-18,+mar/44,XY,dic(5;17)(q11;p11),-18/46,XY,dic(5;17),-18,+mar idiopathic myelofibrosis, chemotherapy
5	M/1	AML	45,XY,hsr(2)(q22),dic(5;17)(q11;p11),der(7)del(7)(q11)hsr(7)(q11),der(12)t(12;19)(p11;q12),-19, +mar embryonal rhabdomyosarcoma, chemotherapy, radiotherapy
6	M/77	AML-M1	47,XY,+14/45,XY,dic(5;17)(q11;p11),dmin/95-96,XXY,-Y,-5,+9,+11,+12,+13,+13, +14,+14,+ 17
7	F/59	RAEB	45,XX,dic(5;17)(q11;p11) acute promyelocytic leukemia, relapse, chemotherapy
8	M/45	AML-M1	46,XY,t(1;15)(p21;q23),t(3;5)(q23;q12),ins(4;12)(q28;p?),dic(5;17)(q11;p11),der(7)t(7;18)(q11;q12) t(14;18)(q12;q23),+8,-14,del(18)(q12q23),add(19)(q23), +21
9	F/63	AML	46,XX,dic(5;17)(q11;p11),-7,der(10)t(10;19)(p11;q11),-19,+2mar
10	M/75	AML	46,XY,-3,dic(5;17)(q11;p11),del(7)(q22q?),+8,+11,-15,+mar
11	M/66	AML-M6	43,XY,der(5)t(5;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
12	F/64	MDS	45,XX,-7/45,XX,dic(5;17)(q11;p11)/44,XX,dic(5;17),der(7)t(7;13)(q11;q14), add(13)(q14),-17/ 44,XX,-3, dic(5;17),der(7)t(3;7)(p14;q32)/44,XX,-3,der(5)t (5;7)(q11;p1?5),dic(5;17), der(7)t(7;16)(p1?5;p13)t(3;7), der(16;17)t(16;17)(p13;p11)ins(16;5)(p13;q11q11),add(21)(q22) adenocarcinoma, chemotherapy, radiotherapy
13	F/50	AML	45,XX,dic(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
14	F/64	AML	45,XX,add(1)(q42),add(4)(q2?5),dic(5;17)(q11;p11),der(6)t(6;12)(q21;q21),-12,+mar/46,idem,+8/ 46,idem,+11, der(11;11)t(11;11)(p15;q25)ins(11;?)(p15;?)/46,idem,+11,der(11;11),+13,-mar,+mar adenocarcinoma, chemotherapy
15	F/73	AML	43,XX,dic(3;22)(p21;p11),dic(5;17)(q11;p11),-7,+8,add(12)(p13),add(14)(p11), -16/44,idem,+mar adenocarcinoma, radiotherapy
16	F/48	MDS	46,XX,t(8;17)(p11;q22) or t(8;17)(p21;q23)/46,XX,del(7)(q22q34)/46,XX,t(2;18)(p21;p11)/ 46,XX,t(2;12)(q11;q21-22),t(11;17)(q13;q25)/45,XX,del(1) (p34p36),dic(5;17)(q13;p11),+8,-18 follicular lymphoma, chemotherapy, radiotherapy
17	M/55	MDS	44,XY,dic(5;17)(q13;p11),dic(19;20)(p13;q11)/45,idem,+mar Hodgkin disease, chemotherapy
18	F/81	MDS	47,XX,del(3)(p21p24),dic(5;17)(q13;p11),+8,+22/48,idem,+X adenocarcinoma, radiotherapy
19	M/58	MDS	45,XY,dic(5;17)(q11;p11),r(7)(p2?2q1?1)/45,idem,dic(5;17),i(9)(p10),del(13)(q12q14)/43,XY, dic(5;17),-7, dic(9;18)(q13;p11)/44,XY,dic(5;17),-7/46,XY,del(11)(q14q23) chronic lymphocytic leukemia, chemotherapy

20	M/73	AML	43,XY,-3,dic(5;17)(q11;p11),-7,+12,t(12;?12)(p13;q13-14),-18,+19,-22/42, idem,-12,del(22)(q11)/ 43,idem,-12,del(22),+del(22)/44,idem,-12,del(22),+del(22),+mar/42,idem,t(9;15)(p2?2;q2?1),-12, del(22)
21	M/57	AML-M7	47,XY,dic(5;17)(q11;p11),-7,-13,add(19)(p13),+4mar
22	M/59	CML	45,XY,dic(5;17)(q11;p11),del(9)(q34) or del(9)(q34q34),t(9;22)(q34;q11)/45,idem,+22/45,XY,t(9;22), der(18) t(17;18)(q11;p11)
23	M/25	AML	44,XY,del(3)(p13),dic(5;17)(q11;p11),-7 Hodgkin disease, chemotherapy, radiotherapy
24	M/8	AML	45,XY,dic(5;17)(q11;p11),del(7)(q22q35)/46,idem,+21/44,idem,der(11;21)t(11;21)(p15;p13) ins(11;?)(p15;?) add(11)(q22) rhabdomyosarcoma, chemotherapy, radiotherapy
25	M/48	AML-M2	45-46,XY,der(5)t(5;17)(q11;q11),r(11;11)(p15q25;q?),-17,+mar/47,idem,+der(5)t(5;17)(q11;q11)/ 44,XY,der(4) t(4;11)(q3?5;q13)ins(4;11)(q3?5;?)t(11;11)(q25;?),der(5)t(5;17),-11,-17/42,XY, dic(5;17)(q11;p11-12),-7,der(11)del(11)(q13q23)dup(11)(q24q22)t(11;12)(q2?2;q22),- 12,der(16)del(16)(q22q24)?dup(16)(q24q24)t(7;16(q11;q24),-18 ?
26	M/54	AML-M6	44,XY,dic(5;17)(q13;p11),-7,add(15)(q24)/44,idem,-dic(5;17),+mar 43,XY,dic(5;17),-7,add(12)(p11),add(15)(q24),-16 56,XY,+Y,+1,+2,add(3)(p13),add(4)(p11),+6,+14,+15,add(15)x2,add(19)(p13), +20,+4mar/113- 116, idemx2,+8,+8,+5mar adenocarcinoma, chemotherapy
27	M/62	AML-M1	43-47,X,-Y,dic(5;17)(q11;p11),der(5;17)t(5;17)t(13;17)(q?14;q?),- 7,der(9)t(9;12)(q34;q?13),+der(10)del(10)(p?)del(10)(q?),-12,der(13;21)(q10;q10),i(13)(q10), der(18)t(14;18)(q?;p?)t(14;21)(q?24;q?11),der(18)t(9;18)(?;p11)t(9;14)t(9;21) Wegeners granulomatosis, chemotherapy
28	M/69	MDS	46,X,t(Y;16)(q12;q?),del(3)(p24p?),del(5)(q31q31),dic(5;17)(q11;p11),dup(19)(q?),+del(21)(q21)/ 48,idem,+18, +19,-dup(19),+22 Hodgkin disease, chemotherapy, radiotherapy
29	F/53	MDS	43,XX,dic(5;17)(q11;p11),dic(6;19)(p2?4;?),-21/43,XX,dic(5;17),-7,ider(21)(q10)del(21)(q22),-22, der(22)t(9;22)(q?;p11) adenocarcinoma, chemotherapy
30	F/86	AML	44,XX,dic(5;17)(q11;p11),-7,der(10)t(10;11)(q25;q22)/43,idem,del(3)(p21),dic(4;7)(q11;q11),+7, der(8)t(4;8) (q21;p21),-12,der(12)t(12;21)(p13;q22),der(21)t(12;21)(q?;q21)/43,idem,del(3), dic(4;7),+7,der(8)t(4;8),dup(11)(q23q23),-12,der(12)t(12;21),der(21)t(12;21) adenocarcinoma, chemotherapy
31	M/73	AML	44,XY,dic(5;17)(q11;p11),der(6)del(6)(p?)del(6)(q?),dup(6)(q?),-7,dup(8)(p?),ins(9;5)(q34;q31q31) Hodgkin disease, chemotherapy, radiotherapy
32	M/39	AML-M1	45,XY,dic(5;17)(q11;p11),+11,-19,der(20)t(19;20)t(19;20)/43,idem,-11,-16/43- 46,idem,dic(3;15)(p11;p11), -4, der(19)t(4;19)(?;q?),der(20)t(19;20)t(4;19) Hodgkin disease, chemotherapy, radiotherapy
33	M/76	MDS	45,XY,dic(5;17)(q11;p11),+6,der(6)t(6;11)(p23;q14- 21)x2,del(7)(q22),dic(15;16)(p11;q11)/45,idem, +del(7)(q31),-del(7)(q22),+dup(7)(q31q31)/45,idem, +15,-dic(15;16),+del(16)(q12),-18 Hodgkin disease, chemotherapy
34	M/72	AML-M1	47-49,XY,der(2;7)dic(2;7)(p23;q11)t(2;12)(q33;q11),dic(5;17)(q11;p12),+8,+r(11)x3, der(12)t(2;12)(p23;q11),+13
35	F/32	MDS	45,XX,dic(5;17)(q11;p11),-7,+r/45,idem,add(14)(p11)
36	F/79	MDS	46,XX,dic(5;7)(q11;p11),idic(5)(q11),r(5),?dic(7;8)(q31;p22),?dic(12;17)(p12;q22)
37	M/69	AML-M2	46,XY,dic(5;17)(q11;p11),-7,+add(11)(q25),+13,del(13)(q31)x2,-16,-17,-18, +3mar
38	M/69	MDS	46,X,t(Y;16)(q12;q?),del(3)(p24p?),del(5)(q13q31),dic(5;17)(q11;p11),dup(19)(q?),+del(21)(q21)/ 48,idem,+18,+19,-dup(19),+22 Hodgkin disease, chemotherapy, radiotherapy
39	M/73	RAEB	44-45,XY,dic(5;17)(q11;p11),+8,-13,-21,+1-2mar/45-47,idem,+13,t(15;18)(q10;q10),+i(21)(q10)
40	M/79	AML-M6	44,XY,add(2)(q21),dic(5;17)(q13;p11),-7,+8,add(12)(p11),-15,-16,+mar

41	M/39	AML	45,XY,-3,r(5)(p14q11),-7,+der(19)t(3;19)(q2?5;q13)/44,XY,-3,dic(5;17)(q12;p11),-7,+mar/ 44,XY, t(3;15) (p2?3;q15),dic(5;12)(q12;p11),-7,add(10)(p13) squamous cell carcinoma, chemotherapy, radiotherapy

Table 1. Reported patients with dic(5;17)(q11-14;p11-13).
Abbreviations: CML, chronic myeloid leukemia; RAEB, Refractory anemia with excess of blasts; AML-M2, Acute myeloblastic leukemia with maturation (FAB type M2); AML-M1, Acute myeloblastic leukemia without maturation (FAB type M1); AML, Acute myeloid leukemia, NOS; AML-M6, Acute erythroleukemia (FAB type M6); MDS, Myelodysplastic syndrome; AML-M7, Acute megakaryoblastic leukemia (FAB type M7). 1. Hagemeijer et al., 1981; 2. Knapp et al., 1985; 3. Huret et al., 1991; 4. Kerim et al., 1991; 5. Heyn et al., 1994; 6. Kwong et al., 1994; 7. Hatzis et al., 1995; 8. Arkesteijn et al., 1996; 9-10. Tosi et al., 1996; 11-24. Wang et al., 1997; 25.Mrozek et al., 2002; 26. Nakamori et al., 2003; 27.Andersen et al., 2005; 28-33.Andersen et al., 2005; 34. Zatkova et al., 2006; 35-37. Herry et al., 2007; 38. Andersen et al., 2008; 39.Lange et al., 2010; 40. Hangai et al., 2013; 41. McNerney et al., 2014.

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

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