Atlas of Genetics and Cytogenetics
in Oncology and Haematology

OPEN ACCESS JOURNAL

INIST-CNRS

Leukaemia Section
Short Communication

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

Adriana Zamecnikova, Soad Al Bahar

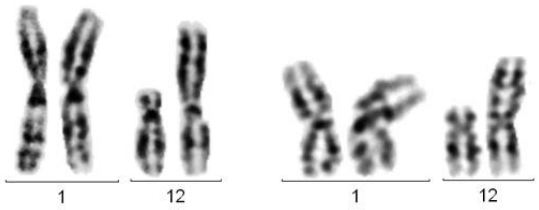
Kuwait Cancer Control Center, Department of Hematology, Kuwait annaadria@yahoo.com

Published in Atlas Database: September 2015
Online updated version : http://AtlasGeneticsOncology.org/Anomalies/t0112q21p13ID1652.html
Printable original version : http://documents.irevues.inist.fr/bitstream/handle/2042/66076/09-2015-t0112q21p13ID1652.pdf
DOI: 10.4267/2042/66076

Abstract

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; González et al., 2004; Gabrea et al., 2008) and 3 with lymphoid malignancies: chronic lymphocytic leukemia (CLL) (Miyamoto 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).

Sex/Age	Disease	Karyotype	Ref.
Myeloid neoplasms			
M/72	AML	46,XY,der(12)t(1;12)(q21;p13)	1
F/59	RA post MM	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,-14,del(20)(p12),add(22)(q12),+3mar	2
M/55	AML-M6	48,XY,+8,der(12)t(1;12)(q21;p13),+mar/48,idem,add(7)(q?)	3
F/1	AML-M5	46,XX,t(9;11)(p22;q23),del(17)(p13),der(22)t(17;22)(p13;q13)/47,XX,+der(9)t(9;11),t(9;11),der(12)t(1;12)(q21;p12)	4
M/66	RAEBI-post MM	45-47,XY,+del(1)(p21),dic(1;7)(p11;q11),der(6)t(3;6)(?;p?22),t(6;21)(p?22;q22),dic(7;13)(p11;p11), der(12)t(1;12)(q21;p13)	5
M	AML-M5	46,XY,der(12)t(1;12)(q11;p11)	6
M	AML-M5	46,XY,der(12)t(1;12)(q11;p11)	7
M/63	RAEBI	47,XY,+8,add(9)(p11),+add(9)(q11),del(20)(p11),+21,add(21)(p11)x2/47,idem,der(1)del(1)(p34)t(1;21)(q12;p12),der(12)t(1;12)(q12;p12),add(14)(p11),-add(21)	8
M/0	AML-M5	47,XY,t(6;19;11)(p22;p13;q23),+der(6)t(6;11)(p22;q23)/48,idem,+8/48,idem,+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),+8	9
F/1	AML-M5	46,XX,der(12)t(1;12)(q12;p13)/46,XX,der(13)t(1;13)(q12;p12)	10
Multiple myeloma			
M	MM	46,XY,del(5)(q13q22),der(10)t(1;10)(q11;p11),t(11;14)(q13;q32),der(14)t(11;14)/46,XY,del(5),t(11;14),der(12)t(1;12)(q11;p11),der(14)t(11;14)	11
M	MM	45,XY,der(12)t(1;12)(q21;p13),-13	12
F	MM	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)(1;17)(q11-12;p13),+18,der(20)t(19;20)(?;q2?2),+21	13
B-cell neoplasms			
M46	CLL	??,XY,del(1)(q?),t(1;10)(q11;p1?5),der(12)t(1;12)(q11;p12)	14
M/40	BL	46,XY,t(8;14)(q24;q32),der(12)t(1;12)(q21;p13),add(14)(q32)/46,idem,add(17)(p?),add(18)(p11)	15
F/79	B-cell neoplasm	48,XX,t(8;22)(q24;q11),der(12)t(1;12)(q21;p13),+17,+mar	16

Table 1. Abbreviations: Ref, reference; M, male; F, female; AML, acute myeloid leukemia; RA, refractory anemia; MM, multiple myeloma; RAEB, refractory anemia with excess of blasts; CLL, chronic lymphocytic leukemia; BL, Burkitt's lymphoma. References: 1. Trent et al., 1983; 2. Pedersen-Bjergaard et al., 1998; 3. La Starza et al., 1999; 4. Odero et al., 2001; 5. Andersen et al., 2005; 6. Fitzgibbon et al., 2005; 7. Raghavan et al., 2005; 8. Gerr et al., 2006; 9. Tuborgh et al., 2013; 10. Parihar et al., 2014; 11. Calasanz et al., 1997; 12. González et al., 2004; 13. Gabrea et al., 2008; 14. Miyamoto et al., 1981; 15. Schoch et al., 1995; 16. Kuroda et al., 2000.

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.

References

Andersen MK, Christiansen DH, Pedersen-Bjergaard J. Centromeric breakage and highly rearranged chromosome derivatives associated with mutations of TP53 are common in therapy-related MDS and AML after therapy with alkylating agents: an M-FISH study. Genes Chromosomes Cancer. 2005 Apr;42(4):358-71

Calasanz MJ, Cigudosa JC, Odero MD, Ferreira C, Ardanaz MT, Fraile A, Carrasco JL, Solé F, Cuesta B, Gullón A. Cytogenetic analysis of 280 patients with multiple myeloma and related disorders: primary breakpoints and clinical correlations. Genes Chromosomes Cancer. 1997 Feb;18(2):84-93

Fitzgibbon J, Smith LL, Raghavan M, Smith ML, Debernardi S, Skoulakis S, Lillington D, Lister TA, Young BD. Association between acquired uniparental disomy and homozygous gene mutation in acute myeloid leukemias. Cancer Res. 2005 Oct 15;65(20):9152-4

Gabrea A, Martelli ML, Qi Y, Roschke A, Barlogie B, Shaughnessy JD Jr, Sawyer JR, Kuehl WM. Secondary genomic rearrangements involving immunoglobulin or MYC loci show similar prevalences in hyperdiploid and nonhyperdiploid myeloma tumors. Genes Chromosomes Cancer. 2008 Jul;47(7):573-90

Gerr H, Gadzicki D, Kreipe H, Schlegelberger B, Wilkens L. Fluorescence in situ hybridization reveals closely correlated results in cytological and histological specimens of hematological neoplasias compared to conventional cytogenetics. Pathobiology. 2006;73(6):271-9

González MB, Hernández JM, García JL, Lumbreras E, Castellanos M, Hernández JM, Fernández-Calvo J, Gutiérrez NC, San Miguel JF. The value of fluorescence in situ hybridization for the detection of 11q in multiple myeloma. Haematologica. 2004 Oct;89(10):1213-8

Kuroda J, Kimura S, Akaogi T, Hayashi H, Abe T, Kobayashi Y, Kondo M. Primary cardiac lymphoma with variant Burkitt-type translocation, t(8;22)(q24;q11) Am J Hematol. 2000 Dec;65(4):327-8

La Starza R, Stella M, Testoni N, Di Bona E, Ciolli S, Marynen P, Martelli MF, Mandelli F, Mecucci C. Characterization of 12p molecular events outside ETV6 in complex karyotypes of acute myeloid malignancies. Br J Haematol. 1999 Nov;107(2):340-6

Miyamoto K, Hamasaki K, Kitajima K, Adachi T, Tanaka T, Sato J. Abnormalities of chromosome no. 1 related to blood dyscrasias: study of 10 cases. Acta Med Okayama. 1981 Apr;35(2):137-41

Odero MD, Carlson KM, Calasanz MJ, Rowley JD. Further characterization of complex chromosomal rearrangements in myeloid malignancies: spectral karyotyping adds precision in defining abnormalities associated with poor prognosis. Leukemia. 2001 Jul;15(7):1133-6

Parihar M, Gupta A, Yadav AK, Mishra DK, Bhattacharyya A, Chandy M. Jumping translocation in a case of de novo infant acute myeloid leukemia. Pediatr Blood Cancer. 2014 Feb;61(2):387-9

Pedersen-Bjergaard J, Timshel S, Andersen MK, Andersen AS, Philip P. Cytogenetically unrelated clones in therapy-related myelodysplasia and acute myeloid leukemia: experience from the Copenhagen series updated to 180 consecutive cases Genes Chromosomes Cancer 1998 Dec;23(4):337-49

Raghavan M, Lillington DM, Skoulakis S, Debernardi S, Chaplin T, Foot NJ, Lister TA, Young BD. Genome-wide single nucleotide polymorphism analysis reveals frequent partial uniparental disomy due to somatic recombination in acute myeloid leukemias Cancer Res 2005 Jan 15;65(2):375-8

Schoch C, Rieder H, Stollmann-Gibbels B, Freund M, Tischler HJ, Silling-Engelhardt G, Fonatsch C. 17p anomalies in lymphoid malignancies: diagnostic and prognostic implications Leuk Lymphoma 1995 Apr;17(3-4):271-9

Trent JM, Davis JR, Durie BG. Cytogenetic analysis of leukaemic colonies from acute and chronic myelogenous leukaemia Br J Cancer 1983 Jan;47(1):103-9

Tuborgh A, Meyer C, Marschalek R, Preiss B, Hasle H, Kjeldsen E. Complex three-way translocation involving MLL, ELL, RREB1, and CMAHP genes in an infant with acute myeloid leukemia and t(6;19;11)(p22 2;p13 1;q23

This article should be referenced as such:

Zamecnikova A, Al Bahar S. der(12)t(1;12)(q11-21;p11-13). Atlas Genet Cytogenet Oncol Haematol. 2016; 20(9):499-501.