

Leukaemia Section

Short Communication

der(1;9)(q10;p10)

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Abstract

Review on der(1;9)(q10;p10), with data on clinics.

Clinics and pathology

Disease

Myeloid malignancies, rarely acute lymphocytic leukemia (ALL), multiple myeloma (MM) and lymphoma.

Phenotype/cell stem origin

10 patients were diagnosed with myeloid malignancies: polycythemia vera (PV) 7 cases (den Nijs van Weert et al., 1989; Swolin et al., 1986; Rege-Cambrin et al., 1991; Boiocchi et al., 2013), myelofibrosis (MF) 2 (Rege-Cambrin et al., 1991; Reilly et al., 1997) and acute myeloid leukemia 1 patient (Bobadilla et al., 2007). There were 4 multiple myeloma MM (Mohamed et al., 2007; Gabrea et al., 2008; Sawyer et al., 2014), 1 ALL (Uckun et al., 1998) and 1 diffuse large B-cell lymphoma (Martin-Subero et al., 2007) cases (Table 1).

Epidemiology

Rare anomaly, found in 6 male and 10 female patients aged 30 to 62 years.

Prognosis

Found in association with leukaemic or myelofibrotic transformation in 7 out of 10 myeloid cases; may represent a poor prognostic indicator with a high propensity to transformation in myeloproliferative disorders.

Cytogenetics

Cytogenetics morphological

Presents as 2 normal chromosomes 1, one normal chromosome 9 and a der(9)t(1;9) chromosome in 4 patients and as +der(1;9)(q10;p10) in 12 cases.

Additional anomalies

Found as the sole abnormality in 1 patient (den Nijs van Weert et al., 1989) and most frequently in combination with numerical anomalies in myeloid cases: loss of chromosomes 5 (Swolin et al., 1986) and/or 7 (Swolin et al., 1986; den Nijs van Weert et al., 1989) in 2 and with extra chromosome 8 in 4 patients (Swolin et al 1986; den Nijs van Weert et al., 1989; Rege-Cambrin et al., 1991).

Numerical gain of chromosome 9, detected in 4 patients (Swolin et al 1986; den Nijs van Weert et al., 1989; Boiocchi et al 2013) is of special interest since it was found only in independent clones that appeared simultaneously or in sequence including the case presenting with trisomy 9 as a sole anomaly who developed an extra der(1;9) during the course of the disease with disappearance of the extra chromosome 9 (den Nijs van Weert et al., 1989).

A t(1;9)(p10;q10) in addition to der(1;9)(q10;p10) chromosome was observed in two patients (Swolin et al., 1986; Reilly et al., 1997). Deletions of the long arms of either chromosome 13 (Rege-Cambrin et al., 1991) or 20 (Swolin et al., 1986) appeared in 3 patients and 2 reported patients showed 12p rearrangements (den Nijs van Weert et al., 1989; Bobadilla et al., 2007).

	der(9)t(1;9)(q11-12;q34)	
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M/35	PCL	44,X,-Y,t(6;8)(q13;p11),der(9)t(1;9)(q12;q34)dup(1)(q12q44),-13	1.
M	MM	45,XY,del(1)(p21p31),der(9)t(1;9)(q11;q34),del(12)(q13q24),-13,add(14)(q32),del(16)(q21),+19/44,idem,del(6)(q16),der(14;15)(q10;q10)add(14)(q32)/90,idemx2	2.
M	MM	46-56,XY,+2,+3,+5,+6,del(6)(q23)x2,+7,+9,der(9)t(1;9)(q12;q34)x2,+11,+15,+17,+19,+mar	3.
F/52	PV	46,XX,del(3)(p21),der(9)t(1;9)(q11;q34) 46,XX,der(9)t(1;9)	4.
F/56	AML-M4	46,XX,der(9)t(1;9)(q11;q34)	5.
M/57	MM	44,XY,der(3)t(1;3)(q21;q29),t(4;14)(p16;q32),der(9)t(1;9)(q12;q34),-10,-13	6.
M/45	CMML	46,XY,der(9)t(1;9)(q11;q34)BCR-ABL1 negative	7.
M	MM	82-92,XXY,-Y,-1,-1,der(1)add(1)(p36)add(1)(q42),-2,-2,del(3)(q21)x2,-4,-4,add(5)(q15),der(5)t(1;5)(q12;q15),add(6)(q21)x2,+7,+7,+7,add(7)(p22),add(7)(q36),der(7)t(1;7)(q12;q32)x3,+8,der(8)t(1;8)(q12;q22)x2,+9,+9,add(9)(p24),der(9)t(1;9)(q12;q34),der(10)t(1;10)(q12;q26),add(11)(p15)x2,-12,-13,del(?13)(q12q22)x3,-14,der(14)t(1;14)(p11;q32)x3,-15,15,add(15)(p11),add(16)(q24),-17,add(17)(p11)x2,+19,+19,-20,+21,add(21)(p11),+22,add(22)(q13),inc	8.
		der(9)(1;9)(q21-q25;q34)	
F/59	AML-M4	46,XX,t(8;16)(p11;p13)/46,idem,der(3)t(3;11)(q27;q13),der(9)t(1;9)(q24;q34)	9.
F/54	AML-M7	48,XX,+5,t(9;22)(q34;q11),+der(22)t(9;22) 47,XX,t(9;22),+der(22)/47,idem,der(9)t(1;9)(q21;q34)/46,XX,del(1)(p11),add(3)(q26),+8,t(9;22),-21 47,XX,t(8;10)(q21;q23),der(9),t(9;22),add(12)(q24),del(13)(q13q32),+der(22)	10.
F	AML	48,XX,der(9)t(1;9)(q23;q34),+11,+21	11.
M/66	CML	46,XY,t(2;17)(p13;q22),der(9)t(1;9)(q21;q34),t(9;22)(q34;q11),der(19)t(19;20)(p13;p11),-20,der(22)t(9;22)/46,X,t(X;20)(q22;q13),t(6;12)(p21;q24). 5 months after PBST	12.
F/0	BAL	46,XX,+1,t(1;15;11;10)(p36;q11;q23;q24),der(1;12)(q10;q10)/46,idem,t(1;12)(p10;p10)/46,idem,t(1;12)(p10;p10),der(9)t(1;9)(q25;q34)	13.
F/1	AML-M7	46,XX,i(7)(q10),der(9)t(1;9)(q25;q34),-16,add(19)(q13),+21c	14.

Table 1. Reported patients with der(1;9)(q10;p10). Abbreviations: PV., polycythemia vera; AML-M4., acute myelomonocytic leukemia; MF., myelofibrosis., AML-M0., acute myeloblastic leukemia with minimal differentiation; AML-M6., acute erythroleukemia; ALL., acute lymphoblastic leukemia; DLBCL., diffuse large B-cell lymphoma; LN., lymph node; MM., multiple myeloma.

1-2. den Nijs van Weert et al., 1989; 3-5. Swolin et al., 1986; 6-7. Rege-Cambrin et al., 1991; 8. Reilly et al., 1997; 9. Bobadilla et al., 2007; 10. Boiocchi et al 2013; 11. Uckun et al., 1998; 12. Martin-Subero et al., 2007; 13. Mohamed et al., 2007; 14-15. Gabrea et al., 2008; 16. Sawyer et al., 2014.

Result of the chromosomal anomaly

Fusion protein

Oncogenesis

Acquired whole-arm chromosome translocations (WAT) of the long arm of chromosome 1 are nonrandom in hematologic malignancies and commonly involve centromeric or paracentromeric sites of chromosome partners. Mostly, these rearrangements are unbalanced leading to genomic imbalances, such as 1q trisomy and monosomy of the whole-arm of the involved chromosome. The unbalanced der(1;9)(q10;p10) is created by translocation between the whole arms of chromosomes 1 and 9 by fusion in their centromeric regions probably as a result of heterochromatin breakage and reunion in centromeric sequences (Sambani et al., 2005). Structural homologies of large blocks of constitutive heterochromatin in

chromosome 1 and 9 centromeric regions might favor such recombination.

der(1;9)(q10;p10) is a relatively rare cytogenetic aberration that presumably occur in myeloproliferative neoplasms (den Nijs van Weert et al., 1989; Rege-Cambrin et al., 1991). In the majority of these cases, it was found as +der(1;9)(q10;p10), therefore leading to trisomy of both 1q and 9p arms. The formation of an extra copies of the entire chromosome arms are likely to be implicated in a neoplastic processes by a gene dosage effect, analogous to numerical aberrations.

The occurrence of +9 in patients with myeloproliferative disorders is of special interest with respect to the JAK2 gene on 9p24.1, suggesting that JAK2 copy number may play a pathogenetic role. This is supported by observation of a series of MPNs patients with t(1;9) describing that patients with either trisomy 9/+9p are invariably JAK2V617F-positive. The majority of these cases also possessed amplification of the gene in addition

to the mutation, thus JAK2 activating mutations may cooperate with 9/9p trisomy. It can be hypothesized that the gain-of-function of JAK2 contributes to the disease phenotype while its enhanced constitutive activation provides a proliferative advantage (Reilly et al., 2008; Campbell et al., 2006). While the timing of the JAK2 mutation is unclear, the occurrence of common trisomies and non-random chromosome deletions in these patients suggests that it may not be the initiating event, but chromosome aneuploidy and gene deletions may precede the acquisition of JAK2 mutations. These data suggest that multiple genetic events may be associated with the development of der(1;9)(q10;p10) that frequently coexists at presentation or later during the further course of the disease. The der(1;9)(q10;p10) is usually present with additional common abnormalities, therefore it is likely to be a secondary event, representing clonal evolution that may play a role in disease progression.

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