

Leukaemia Section

Short Communication

dic(7;12)(p10-p12;p11-p13)

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Abstract

Dicentric chromosomes are recurrent finding in patients with hematological malignancies.

The occurrence of dic(7;12), involving the short arms of chromosomes 7 and 12 is infrequent and has been reported mainly in pediatric B-cell acute lymphoblastic leukemia.

Keywords

Dicentric chromosomes, genomic imbalance, 7p deletion, tumor suppressor genes.

Clinics and pathology

Disease

B-cell acute lymphoblastic leukemia (ALL) mainly.

Etiology

Myeloid malignancies in 3 (3 males aged 52, 53 and 28 years): 1 refractory anemia with excess of blasts (RAEB) (Stevens-Kroef et al 2004), 1 acute myeloblastic leukemia without maturation (AML-M1) (Tapinassi et al., 2008) and 1 chronic myeloid leukemia (CML) (de Oliveira et al., 2012) patient.

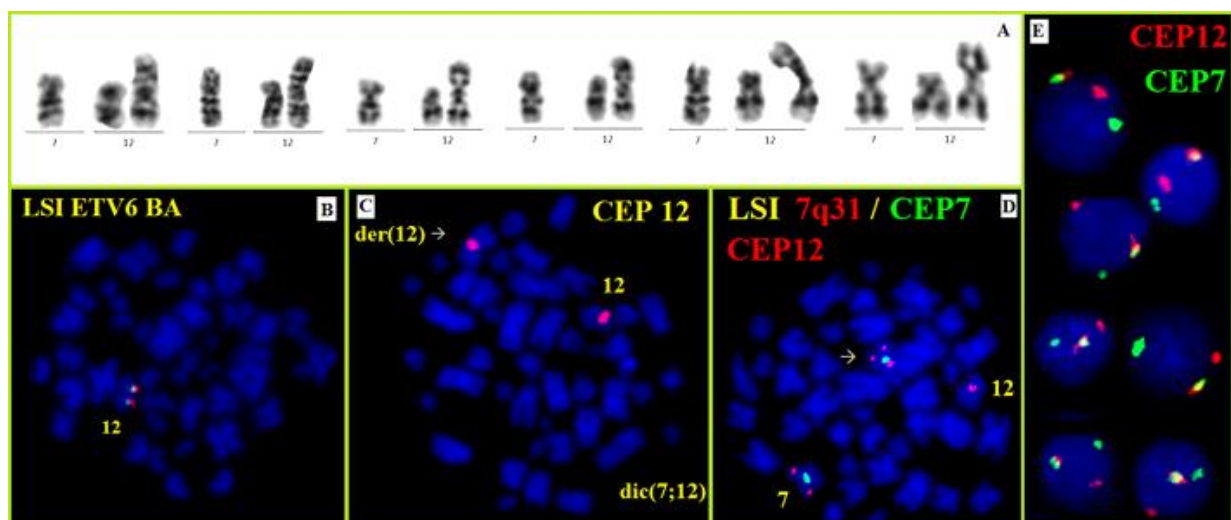


Figure 1. Partial karyotypes with dic(7;12)(p11.2;p11.2) (A). Fluorescence in situ hybridization (FISH) with LSI ETV6 break apart probe (Abott Molecular/Vysis, US) revealing deletion of ETV6 as a result of dicentric chromosome formation (B). Hybridization with CEP12 probe (Abott Molecular/Vysis, US) showed the presence of centromeric 12 signals on normal and dic(7;12) chromosomes (C). Simultaneous hybridization with LSI 7q31/CEP7 and CEP12 probes ((Abott Molecular/Vysis, US) confirmed the presence of chromosome 7 and 12 centromeres on dic(7;12) chromosome on metaphase and interphase cells (DE).

Acute lymphoblastic leukemia in 16 (7 males and 9 females aged 1 to 50 years). Of these, 14 had B-lineage ALL (5 males and 9 females aged 1 to 40 years, median 3 years) (Raimondi et al., 1991; UKCCG 1992; Pui et al., 1993; Snyder et al., 1999; Silva et al., 2002; Raimondi et al., 2003; Russell et al., 2008; Holmfeldt et al., 2013; Olsson et al., 2015; Marincevic-Zuniga et al., 2016), 1 had T-ALL (an 11 years old male) (Raimondi et al., 1991) and one had bilineage or biphenotypic leukemia (a 50 years old male) (Matsumoto et al., 2009).

Epidemiology

19 reported patients (aged 1 to 53 years; median 9 years). Of these, there were 6 adult (aged 28 to 53 years, median 40 years) and 13 pediatric patients (aged 1 to 16 years, median 3 years).

Prognosis

Simultaneous 7p and 12p deletions, found often together with complex karyotypes might indicate genomic instability and an adverse prognostic factor.

Cytogenetics

Cytogenetics morphological

Unbalanced rearrangement; the formation of a dicentric chromosome results in partial 7p/12p monosomies. Most patients had 7p11/12p12 (9 patients) and 7p11/12p11 (8 patients) breakpoints.

Additional anomalies

Sole anomaly in 3 B-ALL patients (Holmfeldt et al., 2013; Olsson et al., 2015; Marincevic-Zuniga et al., 2016). Found in a sideline with del(7)(p11),del(12)(p11) in AML-M1 (Tapinassi et al., 2008), in association with (9;22)(q34;q11),i(12)(q10) in CML (de Oliveira et al., 2012) and complex karyotype in the RAEB patient (Stevens-Kroef et al., 2004). Found with del(1q) in 2 (Raimondi et al., 1991; Raimondi et al., 2003), del(9p) in 1 (Raimondi et al., 1991), del(6q) in 1 (Raimondi et al., 2003), miscellaneous anomalies in 3 (Raimondi et al., 1991; Matsumoto et al., 2009) and with complex karyotypes in 6 ALL patients (UKCCG 1992; Pui et al., 1993; Snyder et al., 1999; Silva et al., 2002; Russell et al., 2008; Olsson et al., 2015).

Result of the chromosomal anomaly

Fusion protein

Oncogenesis

Structural 12p anomalies are observed in a broad spectrum of haematological malignancies including myeloid malignancies and acute lymphoblastic leukemia. Various aberrations result in an abnormal

12p, including balanced translocations, deletions and formation of dicentric chromosomes.

Dicentric chromosomes involving 12p are associated with loss of 12p material that most often include the ETV6 (TEL) gene localized in 12p13.2.

A lot of partner chromosomes are described; of these dic(7;12) involving the short arms of chromosomes 7 and 12 is relatively infrequent.

The genetic consequences of this dicentric chromosome are partial monosomies of 7p and 12p resulting in concomitant deletions of tumor suppressor genes from both chromosomes. dic(7;12) is a rare but recurrent chromosomal abnormality that has been described mainly in acute lymphoblastic leukemia of B-lineage and may represent a distinct cytogenetic subgroup in pediatric ALL.

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