

Case Report Section

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Cryptic t(19;19)(p13.3;q13.2), involving the TCF3/E2A gene, detected and described by molecular cytogenetics in a patient with childhood B-cell progenitor acute lymphoblastic leukemia

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Abstract

Case report on a case of cryptic t(19;19)(p13.3;q13.2), involving the TCF3/E2A gene, detected and described by molecular cytogenetics in a patient with childhood B-cell progenitor acute lymphoblastic leukemia.

Clinics

Age and sex

6 years old male patient.

Previous history

No preleukemia, no previous malignancy, no inborn condition of note
30-day history of fever without an obvious source of infection.

Organomegaly

Hepatomegaly, no splenomegaly, enlarged lymph nodes (in cervical and axillary regions. Ecchymoses and petechiae in lower extremities.), no central nervous system involvement.

Blood

WBC: 1.6 X 10⁹/l

HB: 3.9g/dl

Platelets: 26 X 10⁹/l

Blasts: 0%

Bone marrow: Hypercellular with 45% lymphoblasts

Cyto-Pathology Classification

Cytology

Presence of 45% immature blast cells with a moderate nucleus-to-cytoplasm ratio, evident loose chromatin and nucleoli (1-2 per cell) without granules compatible with FAB classification ALL L2.

Immunophenotype

Blast cells positive for CD19, CD79a, CD22, and TDT; negative for CD45, CD34, CD20, CD10, cyIgM, CD123, NG2, MPO, CD33, CD64, CD15,

CD13, CD65, CD7 and cyCD3. Compatible with B-cell progenitor acute lymphoblastic leukemia (BCP-ALL).

Rearranged Ig Tcr

Not done.

Pathology

Not applicable.

Electron microscopy

Not done.

Diagnosis

Progenitor B-cell lymphoblastic leukemia.

Survival

Date of diagnosis: 09-2012

Treatment: Grupo Brasileiro de Tratamento da Leucemia na Infancia (GBTLI -99) protocol, low-risk arm

Complete remission: complete remission was obtained at D28 of treatment.

Treatment related death: no

Relapse: no

Status: Alive

Last follow up: 08-2013

Survival: 11 months

Karyotype

Sample: Bone marrow

Culture time: 24h

Banding: GTG banding technique

Results

46,XY[20] (Figures 1 and 2)

Karyotype at Relapse

No relapse at that time

Other molecular cytogenetics technics

Fluorescence in situ Hybridization (FISH) using the following locus specific probes: ETV6/RUNX1 (Abbott®), BCR/ABL (Abbott®), MLL break apart (Abbott®), E2A break apart (CytoCell®).

Other molecular cytogenetics results

FISH analysis showed that E2A 3' probe (covering 164 kb 3' of the gene), labeled in green, was rearranged on the "q" arm of the other chromosome 19 (Figure 3A). FISH analysis was negative for ETV6/RUNX1 and BCR/ABL fusion genes and MLL rearrangement. FISH using multicolor banding (MCB) applying the probe set for chromosome 19 (Liehr et al., 2002) also confirmed and refined the reciprocal translocation of chromosomes 19 (Figure 3B). 46,XY.isht(19;19)(p13.3;q13.2)(5'TCF3+;3'TCF3+)



Figure 1: G-banded metaphase with black arrow indicating chromosomes 19.

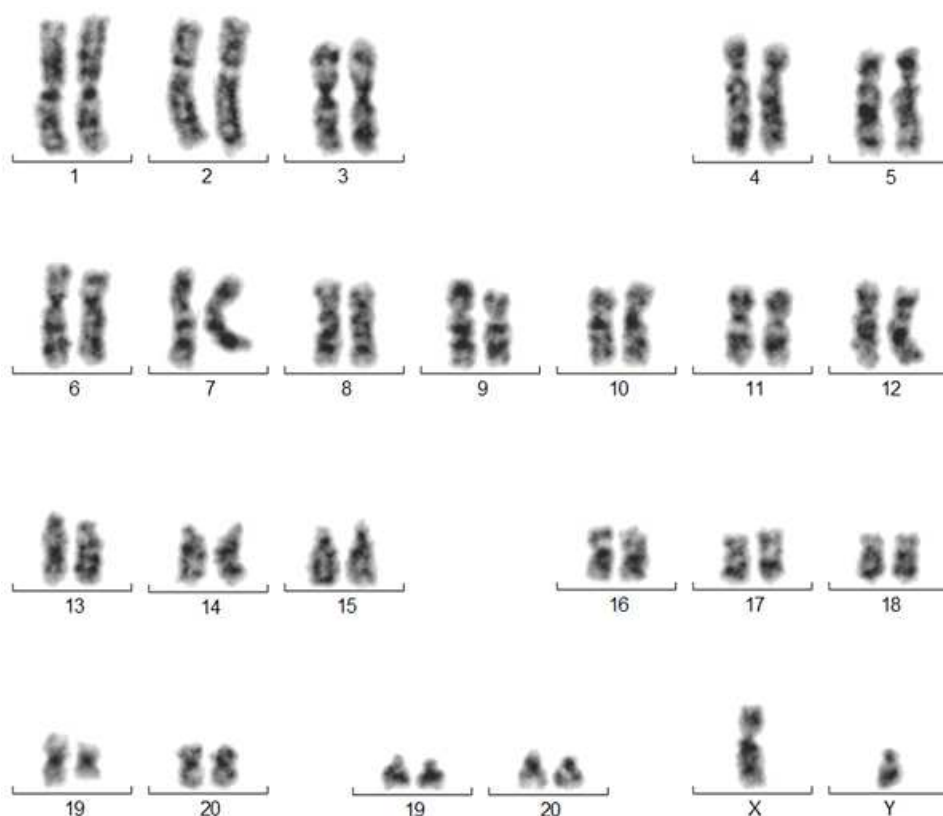


Figure 2: G-banded karyotype.

Other Molecular Studies

Technics:

Semi-quantitative reverse transcription polymerase chain reaction (RT-PCR):

RT-PCR were performed with one microgram of mRNA, treated with DNase Amplification Grade I (Invitrogen) and reverse transcribed with Superscript II Reverse transcriptase® (Invitrogen). Each reaction was carried out with Taq DNA Polymerase (Invitrogen).

The reactions were performed using the following program: 95°C 2 min and 45 cycles at 94°C for 30 sec and 62°C for 1 min and 72°C for 1min. PCR product was analyzed by electrophoresis on 1.5% agarose gel. β -actin was used as control.

The following primers were used:

E2A/PBX1 - Fw, 5'- CACCAGCCTCA
TGCACAAC - 3' / Rev, 5'-
TCGCAGGAGATTCATCACG- 3'; β -ACTIN -Fw,
5'- CAGCAGATGTGGATCAGCAAG -3' / Rev,
5'- GCATTTGCGGTGGACGAT -3'.

Results:

The RT-PCR assay performed, disclosed the presence of E2A-PBX1 gene fusion (Figure 5).

Comments

A t(19;19) has been described as a cryptic abnormality involving E2A(TCF3) gene (Boomer et al., 2001; Brambillasca et al., 1999). Using gene specific probes, FISH is an efficient tool to screen cryptic cytogenetic abnormalities (Boomer et al., 2001; Moorman, 2012). The case presented here had an unremarkable GTG banding study. The chromosomal abnormality was found via FISH screening using the E2A/TCF3 breakapart probe. Because of the rarity and possible prognostic implication of this translocation, we submitted material for MCB analysis (Liehr et al., 2002) and RT-PCR exclude the presence of the cryptic E2A/PBX1 fusion. The results showed that the breakpoint on the 19q13.2 region. This breacpoint observed in the present work differs from that previously described (19q13.4) by Brambillasca, 1999, that described the fusion TCF3/TFPT. Our work provides clinical and cytogenetic data for a child with BCP ALL carrying a novel t(19;19)(p13.3;q13.2). To our knowledge, this is the first report of a case harboring this abnormality. We suggest a putative gene in the breakpoint region might be involved in leukemogenesis.

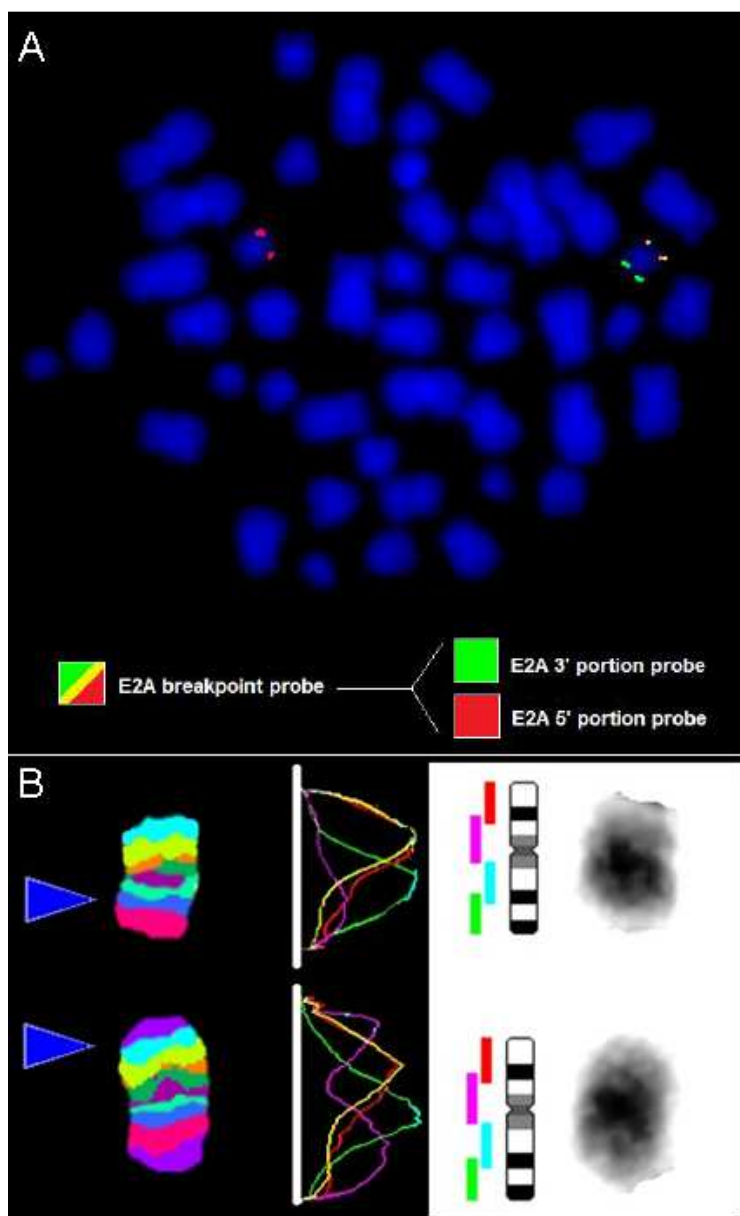


Figure 3: A) E2A dual color break apart probe showing E2A 3' portion rearranged at the q arm of the other chromosome 19. B) MCB for chromosome 19.

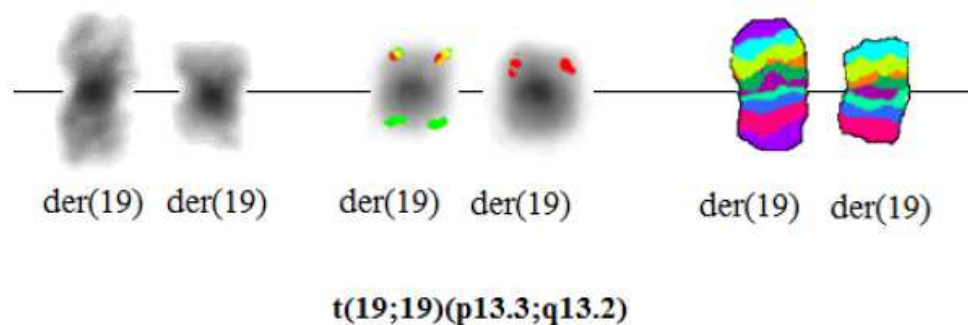


Figure 4: Partial karyotype showing G-banded, FISH and MCB chromosomes.

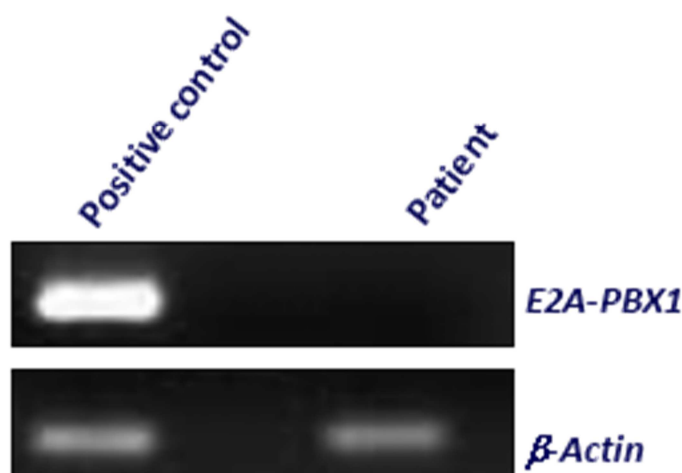


Figure 5: Semi-quantitative RT-PCR analysis to detect E2A/PBX1 expression. E2A/PBX1 were expressed in a patient with t(1;19) (positive control). The E2A/PBX1 fusion was not detected in the patient with t(19;19). β-actin was used as control.

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