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Case Report Section

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Trisomy 16 and 18 in acute lymphoblastic leukemia patient with ETV6-RUNX1 rearrangement

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Clinics

Age and sex
3 years old female patient.

Previous history
No preleukemia. No previous malignancy. No inborn condition of note.

Organomegaly
No hepatomegaly, no splenomegaly, no enlarged lymph nodes, no central nervous system involvement.

Blood

WBC : 3.2 X 10^9/l
HB : 9.8g/dl
Platelets : 52 X 10^9/l
Blasts : 29 Neutrohils 8%, Lymphocytes 61%, Eosinophils 2%, atypical lymphocytes 29%.
Bone marrow: Hypercellular, with 70% lymphoblasts replacing normal marrow elements.

Cyto-Pathology Classification

Cytology
ALL

Immunophenotype
Positive for CD10 (90%), CD19 (81%), CD22 (81 %), 13 (61%), 33 (82%), 79a (38%), 34 (82%), HLDR (90%) and TdT (56%)

Diagnosis
B-lineage ALL

Survival

Date of diagnosis: 01-2011. Last follow up: 01-2011.

Karyotype

Sample: Bone marrow

Culture time: 24h

Banding: G-band

Results
48,XX,+16,+18

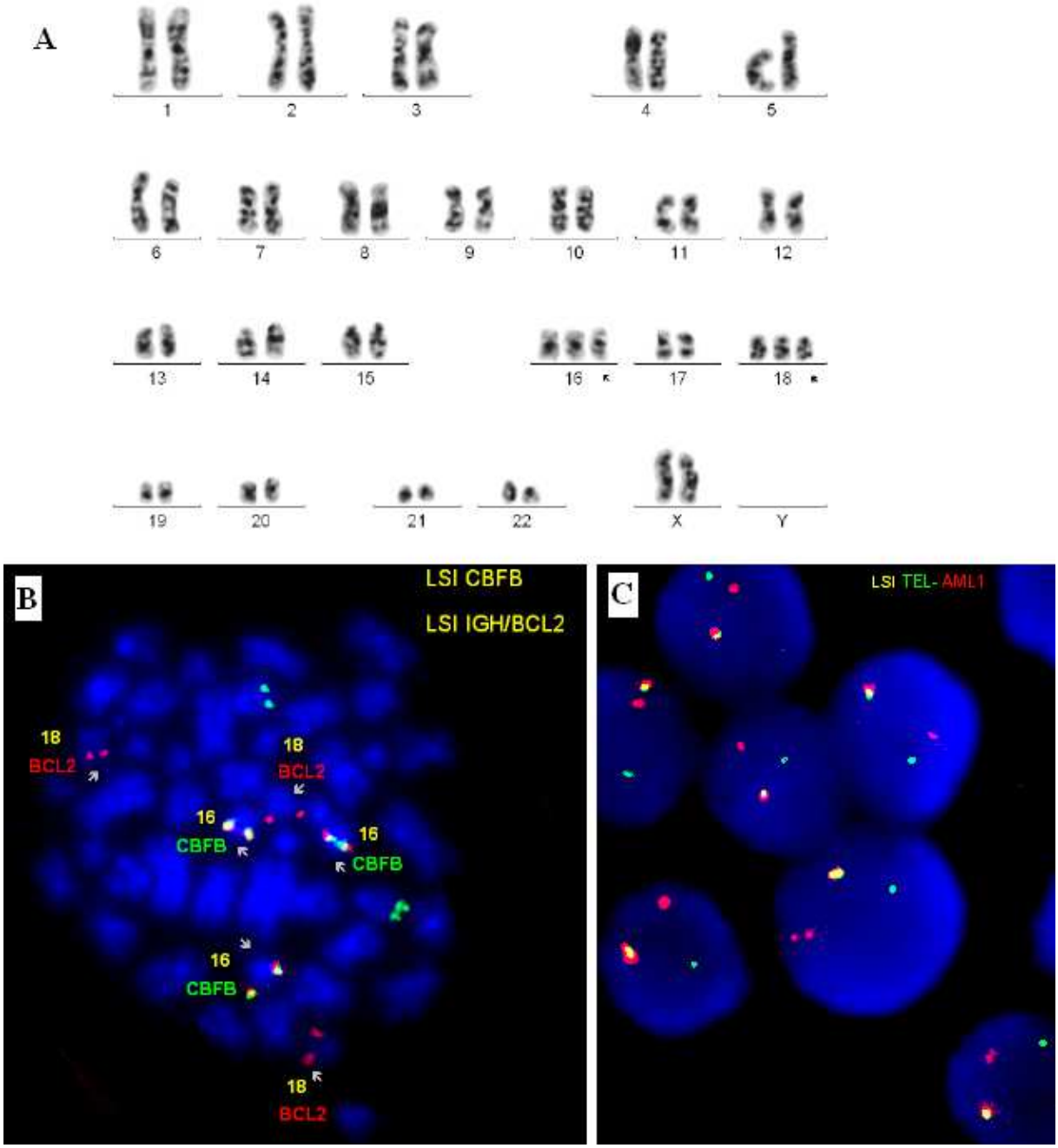
Other molecular cytogenetics technics
Fluorescence in situ hybridization with LSI TEL-AML1 (ETV6-RUNX1), LSI IGH/BCL2 and LSI CBFB probes.

Other molecular cytogenetics results
Applying the LSI TEL-AML1 probe on bone marrow cells we detected in 70% of cells fusion signal for TEL-AML1. Applying the LSI IGH/BCL2 and LSI CBFB probes on metaphases we detected 3 copies for BCL2 and CBFB confirming the presence of extra chromosomes 16 and 18.

Other Molecular Studies

Technics: RT-PCR for TEL-AML1

Results: Positive



Karyotype of the patient showing the presence of extra chromosomes 16 and 18 (A). Fluorescence in situ hybridization studies with LSI IGH/BCL2 and CBFB probes showing the presence of 3 copies of BCL2 and CBFB probes on chromosomes 16 and 18 (B). Hybridization with LSI TEL-AML1 (ETV6-RUNX1) probe showing the fusion signals on interphase cells (C).

Comments

Current evidence suggests that in childhood acute lymphoblastic leukemia (ALL) with t(12;21), while the translocation may initiate the leukemic process, secondary genetic events are believed to be pivotal in disease promotion. We report a case of a patient displaying trisomy 16 and 18 as the sole cytogenetic anomaly detected by karyotyping. The patient, a previously healthy 3 years old female presented with fever and pancytopenia. Immunophenotyping showed B-lineage ALL, with aberrant expression of myeloid markers. Chromosome analysis performed at diagnosis revealed extra copies of chromosomes 16 and 18 in all the 20 examined metaphases. Fluorescence in situ studies revealed ETV6-RUNX1 fusion signal in 70% of cells and the rearrangement was confirmed by reverse-transcriptase polymerase chain reaction. While extra copies of chromosomes 16 and 18 may be observed in pediatric ALL patients with hyperdiploid karyotypes suggesting that they may exists as an evolutionary change, isolated trisomy 16 or 18 have been reported only rarely. A case similar to ours was previously reported in a child cytogenetically characterized by an

isolated trisomy 16 and ETV6-RUNX1 fusion. Our case together with the previously reported case of B-cell ALL with ETV6-RUNX1 rearrangement suggests that trisomy of chromosome 16 and is an important additional or secondary genetic event in childhood ALL with ETV6-RUNX1 fusion. In addition, several cases of pediatric ALL with isolated trisomy 16 or 18 were reported potentially harboring the ETV6-RUNX1 rearrangement. As the translocation t(12;21) usually escapes diagnosis on conventional karyotyping, our case further reinforces the importance of fluorescence in situ hybridization studies in pediatric leukemias to reveal cryptic genomic rearrangements in addition to visible cytogenetic changes.

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