Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL

INIST-CNRS

Case Report Section

A new case of acute lymphoblastic leukemia with der(X)t(X;8)(q28;q11.2)

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Published in Atlas Database: July 2016

Online updated version : http://AtlasGeneticsOncology.org/Reports/0X08q28q11GindinaID100088.html

Printable original version : http://documents.irevues.inist.fr/bitstream/handle/2042/69004/07-2016-0X08q28q11GindinaID100088.pdf

DOI: 10.4267/2042/69004

Abstract

Case report on a new case of acute lymphoblastic leukemia with der(X)t(X;8)(q28;q11.2).

Clinics

Age and sex: 19 year(s) old male patient

Previous history: no preleukemia , no previous malignancy , no inborn condition of note

Organomegaly: hepatomegaly ; splenomegaly ; enlarged lymph nodes (Few reddish skin nodules 5-7 mm in diameter); central nervous system involvement (A tumor-forming mass located in temporal lobe of brain at post-transplant relapse.)

Blood

WBC: 1.7X 10^9/l
HB: 9.0g/dl
Platelets: 296X 10^9/l
Bone marrow: Bone marrow smears showed hypercellular bone marrow with 54.4% blasts. They were negative for myeloperoxidase, whereas most of them positive for PAS stain. The cytoplasm of blasts was narrow and basophilic. Blasts had rounded nucleus and finely dispersed chromatin with well-contoured nucleoli. Erythropoiesis and myelopoiesis were decreased. Erythropoiesis had signs of megaloblastosis. Megakaryocytopoiesis: hypolobular and polyploid megakaryocytes.

Cyto-Pathology Classification

Phenotype
B-ALL
Immunophenotype
Positive for CD34, CD10, CD19, CD20, CD38.
Rearranged Ig Tcr : Not performed.
Pathology : Histopathology of the skin nodules was remarkable for interstitially located groups of small- and middle-sized lymphoid blast-like cells, which were positive for TdT, PAX-5, CD20, CD10, negative for T-cell and myeloid markers and had a very high proliferation rate (Ki-67 index above 90 %).
C-myc oncogene product was additionally assessed with immunohistochemistry (clone Y69). Over 90% of blast cells in the skin appeared to be positive for ?-myc, although staining pattern was markedly heterogeneous.
The brain tissue (at post-transplant relapse) contained a dense cellular infiltrate composed of middle-sized PAS-positive blasts with oval or round nuclei, containing 2-3 small nucleoli. Tumor cells were uniformly positive for TdT, CD19, PAX-5, and CD79a and had a very high Ki-67 proliferation index. C-myc oncogene product was demonstrated in over 85% of cells with heterogeneous staining pattern, compatible with indirect c-myc up-regulation.

Electron microscopy : Not performed.

Diagnosis Common acute lymphoblastic leukemia

Survival

Date of diagnosis 09-2012

Treatment: Treatment was started according to ALL-2009 protocol, containing Daunorubicin, VIncristine and L-asparaginase. CNS prophylaxis therapy consisted intrathecal treatment, whereas cranial irradiation was not used.

Complete remission: obtained

Treatment related death: no

Relapse: Yes. Complex medullar and CNS extramedullary relapses were diagnosed repeatedly on 10 and 13 months after remission.

The patient received allogeneic HSCT on 04/2014. Complete remission was achieved on 06/2014. Isolated post-transplant CNS relapse was diagnosed on 11/2014.

Phenotype at relapse : Positive for CD34, CD10, CD19, CD20, CD38.

Status: Dead

Survival: 29 months

Karyotype

Sample Bone marrow aspirate, brain tumor mass (by stereotactic brain biopsy at post-transplant relapse)

Culture time 24 h, without stimulating agents.

Banding GTG

Results 45,Y,der(X)t(X;8)(q28;q11.2)[20]

Karyotype at relapse

45,Y,der(X)t(X;8)(q28;q11.2)[20]

Other molecular cytogenetics technics

Fluorescence in situ hybridisation (FISH) with whole painting probes for 8 and X chromosomes (Metasystems, Germany). Multicolor banding, using a multicolor probe for chromosome 8 (Metasystems, Germany).

Other molecular cytogenetics results

The unbalanced translocation der(X)t(X;8)(q28;q11.2) was revealed in all metaphases.

Other molecular studies

Technics RT-PCR

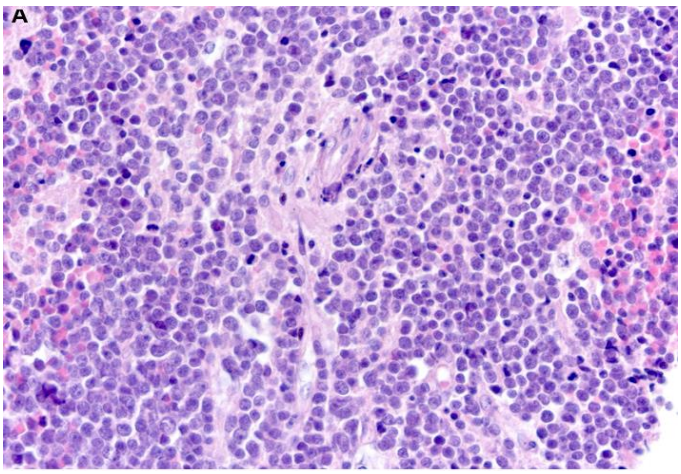
Results Leukemic cells were negative for t(1;19)E2A-PBX1, del(1)SIL-TAL1, t(12;21) TEL-AML1, and t(9;22) BCR-ABL.

Comments

Here we report a new case of ALL with extremely rare abnormality der(X)t(X;8)(q28;q11.2), which resulted in a partial 8q trisomy. At the first time a case with der(X)t(X;8)(q28;q11.2) was reported in a 4-year-old child with Ph-positive ALL who has not achieved complete continuous remission [Kaleem et al, 2000].

This patient had other recurrent chromosomal abnormalities, such as t(8;14)(q11.2;q32), t(9;22)(q34;q11) and add(17)(p13). It allows to consider, that the der(X)t(X;8) might be a secondary genetic event. As for our finding is concerned, it seems to be primary event, which is responsible for post-transplant isolated CNS relapse.

Identical chromosome abnormalities in leukemic cells at diagnosis and in the cells from brain tumor-forming relapse support the origin of both from common leukemic clone. c-Myc is one of the genes located on 8q which may be implicated in disease biology. Immunohistochemical staining for c-myc protein showed positivity of >85% of leukemic cells (at disease onset and at relapse), although with markedly heterogeneous staining pattern, compatible with indirect c-myc up-regulation. The latter, in turn, could increase proliferative potential of leukemic cells as well as their resistance to chemotherapy. Finally, trisomy 8 in ALL patients is considered to be indicative of poor prognosis [Garipidou et al, 1990].



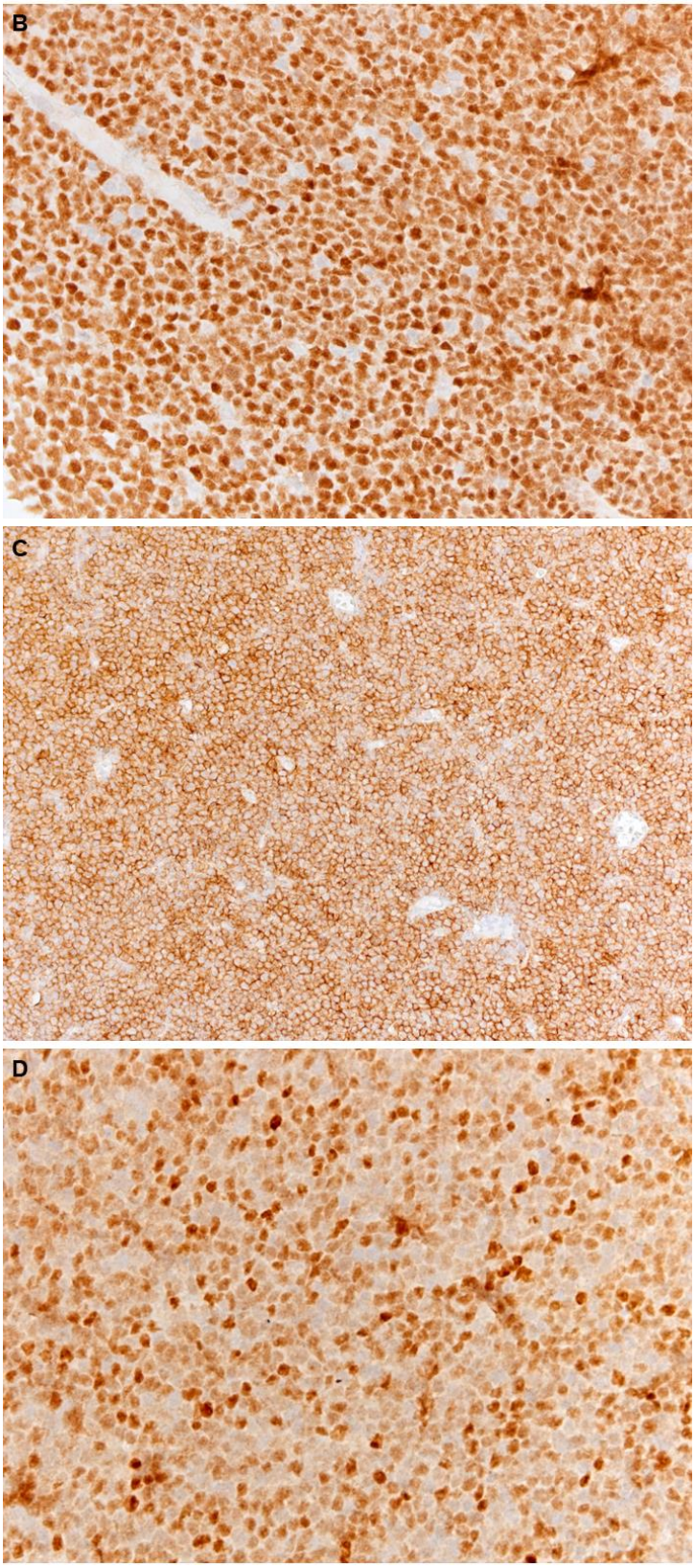


Figure 1: Histopathological findings in tumor-forming ALL relapse in the brain. Neoplastic cells with lymphoblastic morphology form diffuse dense infiltrate in the brain tissue (A), they are uniformly positive for TdT (B), CD19 (C), and heterogeneously express c-myc (D). Hematoxylin and eosin staining, 400× original magnification (A); IHC for TdT, 400? original magnification (B); IHC for CD19, 200× original magnification (C); IHC for c-myc 400× original magnification (D).

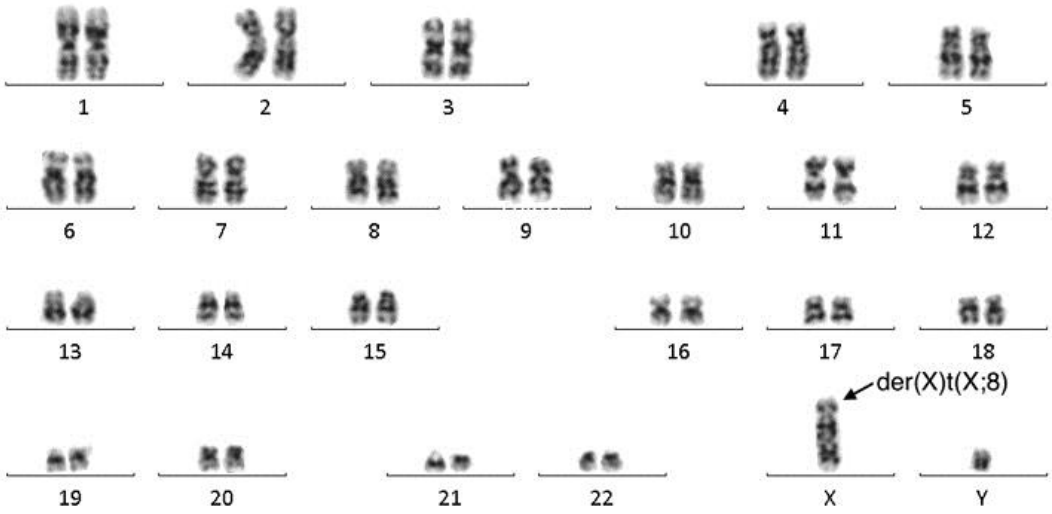


Figure 2: GTG-banded karyotype showing the derivative der(X)t(X;8)(q28;q11.2)

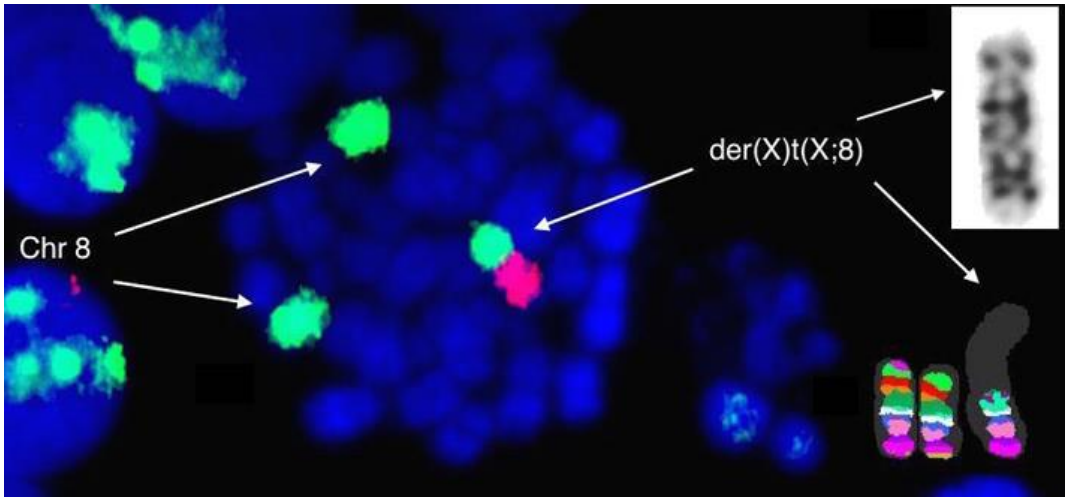


Figure 3: GTG-banding showing the derivative X chromosome; FISH with whole painting probes showing two normal chromosomes 8 (green color) and the derivative der(X)t(X;8) (red and green colors). Multicolor banding of two normal chromosomes 8 and the derivative X chromosome.

References

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This article should be referenced as such:

Gindina T, Mamayev N, Baykov V, Slesarchuk O, Rudakova T, Babenko E, Afanasyev B. A new case of acute lymphoblastic leukemia with der(X)t(X;8)(q28;q11.2). Atlas Genet Cytogenet Oncol Haematol. 2017; 21(11):434-437.