

Case Report Section

Paper co-edited with the European LeukemiaNet

AML with t(7;21)(p22;q22) and 5q abnormality, a case report

Jianling Ji, Eric Loo, Carlos A Tirado

Department of Pathology and Laboratory Medicine, David Geffen UCLA School of Medicine, Los Angeles, CA, USA (JJ, EL, CAT)

Published in Atlas Database: March 2014

Online updated version : <http://AtlasGeneticsOncology.org/Reports/t0721p22q22JiID100077.html>
DOI: 10.4267/2042/54142

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2014 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Abstract

Case report and literature review on AML with t(7;21)(p22;q22) and 5q abnormality.

Clinics

Age and sex

57 years old female patient.

Previous history

No preleukemia, no previous malignancy, no inborn condition of note, no main items.

Organomegaly

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

Blood

WBC: 2.32 X 10⁹/l

HB: 6.9g/dl

Platelets: 170X 10⁹/l

Blasts: 0%

Bone marrow: 25%

Cyto-Pathology Classification

Immunophenotype

CD10 (partial), CD11b (partial), CD13, CD14 (partial), CD15 (partial), CD16 (partial), CD22 (partial), CD34 (partial), CD36 (partial), CD38, CD56 (partial), CD64 (partial), CD117 (partial), HLA-DR (bright), icCD22 (partial), and MPO (partial) with aberrant expression of CD7 (partial).

Rearranged Ig Tcr

Not performed.

Pathology

Acute myeloid leukemia, not otherwise specified (AML, NOS), with monocytic differentiation.

Electron microscopy

Not performed.

Diagnosis

Acute myeloid leukemia, not otherwise specified (AML, NOS); Acute myelomonocytic leukemia subtype.

Survival

Date of diagnosis: 02-2013

Treatment

Following diagnosis, the patient was seen at an outside institution for treatment and was placed on Revlimid therapy as opposed to induction chemotherapy for about 5 months without improvement or significant deterioration of her blood counts. She was referred to our institution to be evaluated for allogenic stem-cell transplantation. A repeat bone marrow biopsy (~6-7 months post diagnosis) confirmed persistent AML, and the cytogenetic studies were performed. The patient was then started on 7+3 AML induction (Cytarabine 320 mg IV continuous days 1-7, Idarubicin 19 mg IV on days 3-6). A day 16 repeat bone marrow biopsy showed persistent presence of abnormal myeloblasts. Biopsy about 6 weeks following induction therapy showed remission with no excess or abnormal myeloblasts. She was subsequently admitted and completed her first cycle

of consolidation chemotherapy with high-dose cytarabine (3 gm/m² IV q 12 hours on days 1, 3, 5 for 6 doses).

Complete remission was obtained.

Treatment related death: no

Relapse: no.

Status: Alive. Last follow up: 12-2013.

Survival: 9 months

Karyotype

Sample: Bone marrow aspirate

Culture time: 24h without stimulating agents

Banding: GPG

Results

Analysis of 20 metaphase cells revealed an abnormal female karyotype with additional material of unknown origin at 5q13 leading to partial deletion of 5q in 5/20 metaphase cells examined. The karyotype was described as: 46,XX,add(5)(q13)[5]/46,XX[15].

Other molecular cytogenetics technics

Fluorescence in situ hybridization (FISH) using the LSI RUNX1(AML1)/RUNX1T1(ETO) Dual Color Translocation Probe and LSI EGR1/D5S23, D5S721 Dual Color Probe Set (Abbott Molecular, USA) were performed.

Other molecular cytogenetics results

Split of the RUNX1 gene was detected in the

interphase nuclei (three green signals) in 235/300 nuclei, and 5q deletion was detected (two green one orange signal pattern) in 19/300 nuclei.

Subsequent metaphase FISH on previously G-banded slides was performed by using RUNX1/RUNX1T1 and 7p sub-telomere probe.

The cryptic translocation t(7;21) was identified.

Based on the metaphase FISH study, the final ISCN was characterized as: 46,XX,add(5)(q13)[5]/46,XX[15].ish t(7;21)(p22;q22)(RUNX1+; VIIyRM2185+)[2].

Other Molecular Studies

Technics:

DNA was isolated by routine methods and subjected to quantitative real-time polymerase chain reaction using allele-specific primers complementary to the mutated and wild-type sequences of the JAK2 gene.

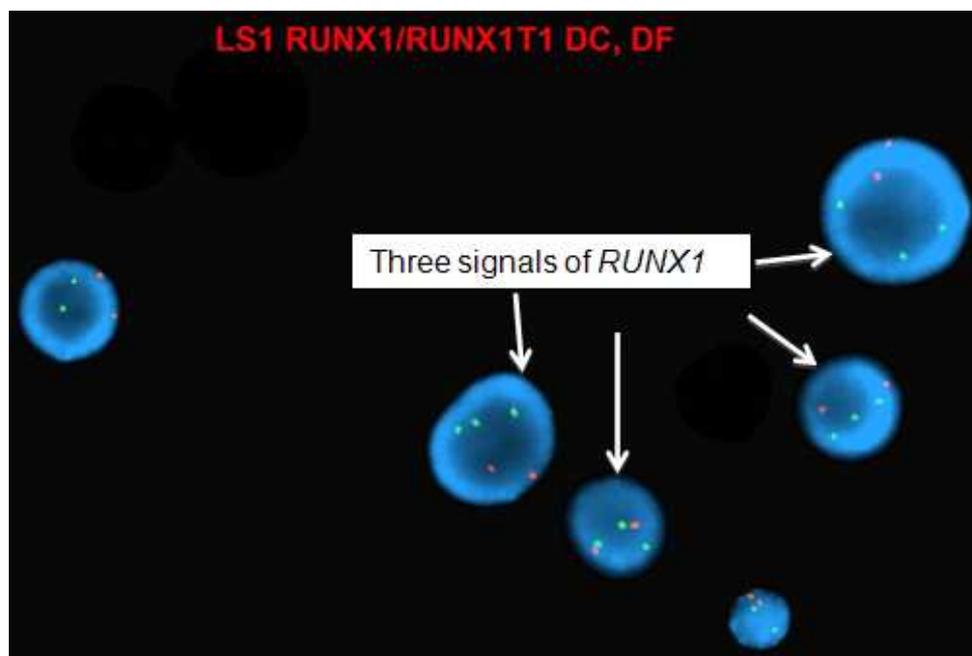
Results:

Negative for JAK2 mutation V617F.

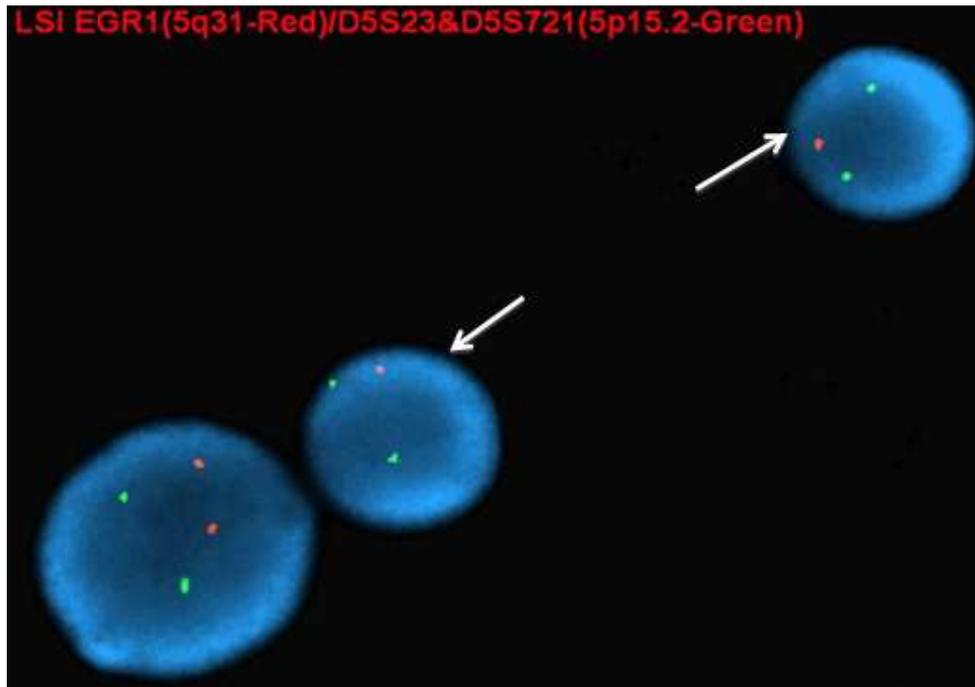
Other Findings

Note:

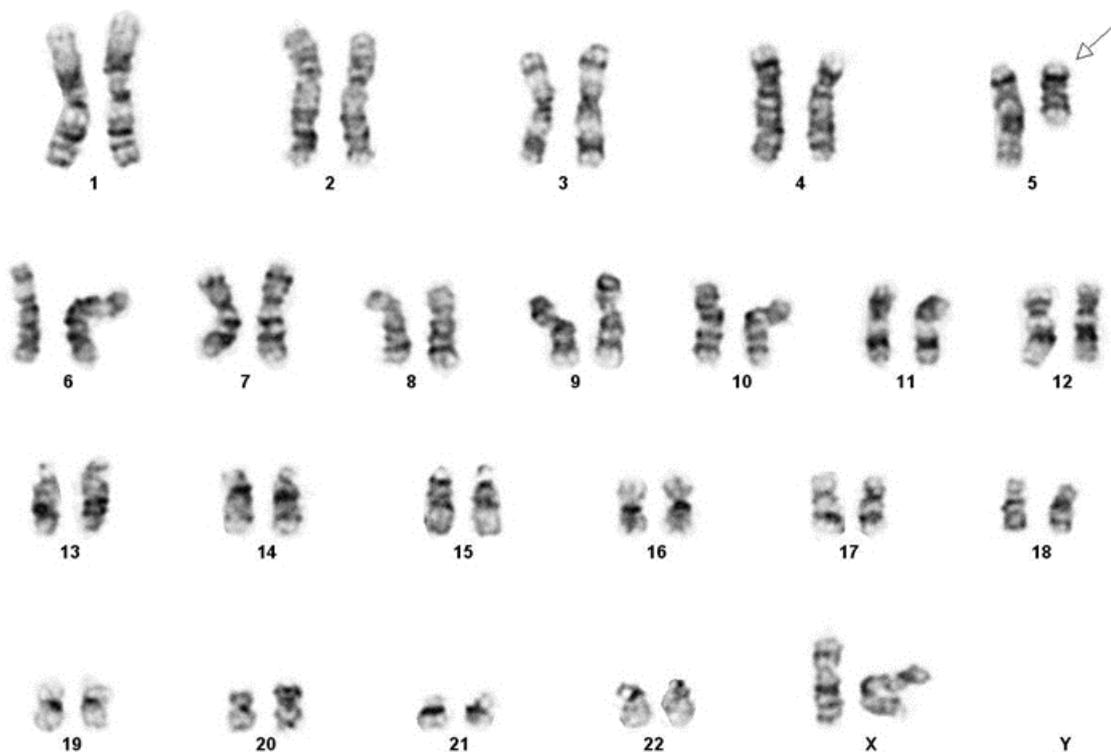
The previous FISH studies on G-banded metaphases showed that the AML1 signal was split and moved to 7p, and the subtelomeric probes for 7p/q showed that the 7p signal moved to 21q, thus, establishing the t(7;12).



Interphase FISH with three signals of RUNX1 (green) and two signals of RUNX1T1 (orange).



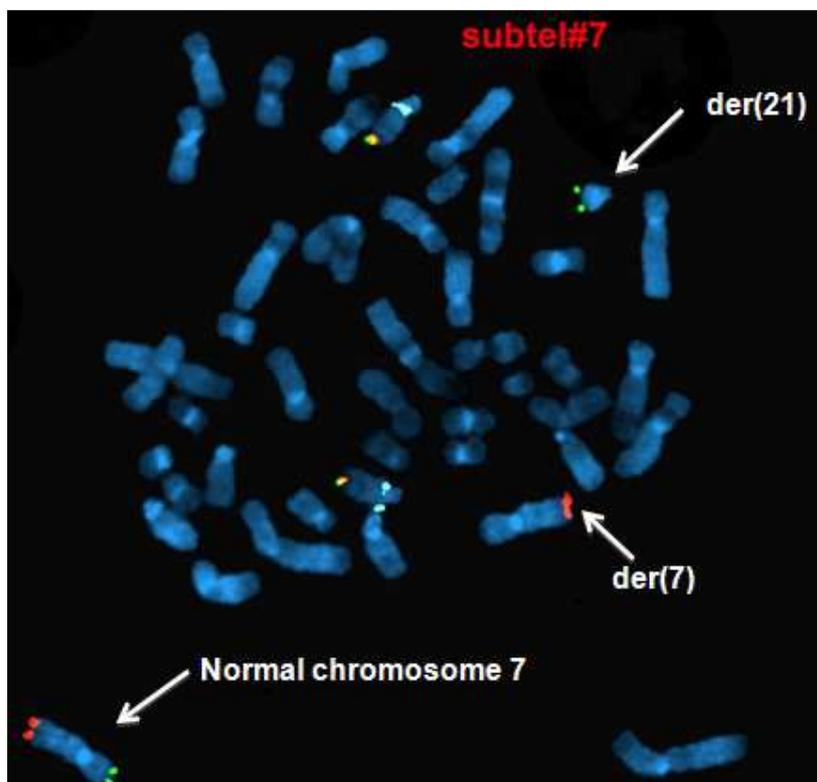
Interphase FISH with two signals of 5p15.2 region (green) and one signal of EGR1 (orange) suggests loss of 5q.



Karyotype on the bone marrow aspirate showing additional material of unknown origin attached at 5q13 leading to 5q loss.



The sequential FISH study on a previously G-banded metaphase with LSI RUNX1/RUNX1T1 probe showing the green signals of RUNX1 on der(7), der(21) and normal chromosome 21, respectively. Two normal orange of RUNX1T1 are seen on the chromosomes 7.



FISH with TelVysion 7p (green, on the sub-telomere region of 7p), 7q (orange, on the sub-telomere region of 7q) and chromosome 14 (yellow and aqua) showing one green signal of 7p on der(21), and the der(7) is missing a green signal. Two normal chromosomes 14 are seen as indicated by the signal pattern (one yellow and one aqua signals on two normal chromosomes 14 respectively).

Comments

We present a new case of AML, NOS with monocytic differentiation (myelomonocytic leukemia) which was shown to carry a cryptic t(7;21)(p22;q22) and 5q loss.

The cryptic translocation t(7;21)(p22;q22) involving RUNX1 and presumably USP42 is a rare recurrent abnormality in AML (Paulsson et al., 2006) and shows association with 5q abnormalities. RUNX1 codes for a transcription factor in the 'Runt domain' gene family and is a regulator of hematopoiesis.

The gene USP42 is involved in the ubiquitin pathway, and is fused to the 3' region of the RUNX1 gene in this translocation.

A recent study evaluated 397 consecutive AML patients with RUNX1 FISH probes and identified 3 patients with t(7;21)(p22;q22), suggesting a relative incidence in about 1% of AML cases (Jeandidier et al., 2012).

Nine previously reported cases have been identified on literature review (see references below) with a broad age of onset (7-68 years, median 39), many with monocytic differentiation, frequently aberrant immunophenotypic antigen expression (often with CD7 and/or CD56), and generally poor response to induction chemotherapy.

Long term survival data are limited at present.

Our presented case also had evidence of persistent leukemia after 6 months of initial treatment with Revlimid (at another institution), but achieved complete remission by morphology, flow, and cytogenetics after standard 7+3 AML induction chemotherapy.

She has since completed her first cycle of consolidation chemotherapy (high-dose Cytarabine) without incident. She is alive and in remission as of 9 months from diagnosis.

References

Paulsson K, Békássy AN, Olofsson T, Mitelman F, Johansson B, Panagopoulos I. A novel and cytogenetically cryptic t(7;21)(p22;q22) in acute myeloid leukemia results in fusion of RUNX1 with the ubiquitin-specific protease gene USP42. *Leukemia*. 2006 Feb;20(2):224-9

Foster N, Paulsson K, Sales M, Cunningham J, Groves M, O'Connor N, Begum S, Stubbs T, McMullan DJ, Griffiths M, Pratt N, Tauro S. Molecular characterisation of a recurrent, semi-cryptic RUNX1 translocation t(7;21) in myelodysplastic syndrome and acute myeloid leukaemia. *Br J Haematol*. 2010 Mar;148(6):938-43

Giguère A, Hébert J. Microhomologies and topoisomerase II consensus sequences identified near the breakpoint junctions of the recurrent t(7;21)(p22;q22) translocation in acute myeloid leukemia. *Genes Chromosomes Cancer*. 2011 Apr;50(4):228-38

Gindina T, Barkhatov I, Boychenko E, Garbuzova I, Vlasova M, Nikolaeva E, Petrova I, Ovechkina V, Shorstova T.. A new case of Acute Myeloid Leukemia with semi-cryptic t(7;21)(p22;q22). *Atlas Genet Cytogenet Oncol Haematol*. April 2012. URL: <http://AtlasGeneticsOncology.org/Reports/t721p22q22GindinalD100064.html>.

Jeandidier E, Gervais C, Radford-Weiss I, Zink E, Gangneux C, Eischen A, Galois AC, Helias C, Dano L, Cammarata O, Jung G, Harzallah I, Guerin E, Martzloff L, Drenou B, Lioure B, Tancredi C, Rimelen V, Mauvieux L.. A cytogenetic study of 397 consecutive acute myeloid leukemia cases identified three with a t(7;21) associated with 5q abnormalities and exhibiting similar clinical and biological features, suggesting a new, rare acute myeloid leukemia entity. *Cancer Genet*. 2012 Jul-Aug;205(7-8):365-72. doi: 10.1016/j.cancergen.2012.04.007.

Panagopoulos I, Gorunova L, Brandal P, Garnes M, Tierens A, Heim S.. Myeloid leukemia with t(7;21)(p22;q22) and 5q deletion. *Oncol Rep*. 2013 Oct;30(4):1549-52. doi: 10.3892/or.2013.2623. Epub 2013 Jul 18.

This article should be referenced as such:

Ji J, Loo E, Tirado CA. AML with t(7;21)(p22;q22) and 5q abnormality, a case report. *Atlas Genet Cytogenet Oncol Haematol*. 2014; 18(10):784-788.
