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

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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 10^9/l
HB: 6.9g/dl
Platelets: 170X 10^9/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)/RUNXT1(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/RUNXT1 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+; VJyRM2185+)[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).

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Interphase FISH with three signals of RUNX1 (green) and two signals of RUNXT1 (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.
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The sequential FISH study on a previously G-banded metaphase with LSI RUNX1/RUNXT1 probe showing the green signals of RUNX1 on der(7), der(21) and normal chromosome 21, respectively. Two normal orange of RUNXT1 are seen on the chromosomes 8.

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


This article should be referenced as such:

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