

Case Report Section

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t(6;22)(p21;q11.2) arising at second relapse in a patient with t(8;21)-positive acute myeloid leukemia

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Clinics

Age and sex

60 years old male patient.

Previous history

Preleukemia. The patient was diagnosed with FLT3 negative, NPM1 negative AML in March of 2010. His karyotype at diagnosis was 46,XY, t(8;21)(q22;q22). He was treated with cytarabine and idarubicin for induction and cytarabine and daunorubicin for consolidation. He relapsed in November, 2010 and received mitoxantrone, etoposide, and cytarabine for re-induction. Cytogenetics performed at the time of this first relapse continued to demonstrate t(8;21)(q22;q22) as the sole cytogenetic abnormality. Upon evaluation in April, 2011 for potential stem-cell transplant, the bone marrow biopsy described in this study confirmed that the patient's acute myeloid leukemia had relapsed for a second time.

No previous malignancy, no inborn condition of note.

Organomegaly

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

Blood

WBC : 7.3 X 10⁹/l

HB : 15.0 g/dl

Platelets : 93 X 10⁹/l

Blasts : 0%

Bone marrow : 60 Hypercellular bone marrow (60-70%) with extensive involvement by leukemia. Histologic sections demonstrate focal sheets of CD34+, CD117+ immature cells. The blasts identified on histologic sections of the marrow are under-represented on the aspirate, which shows 1% blasts, and the flow cytometry specimen, which demonstrates 3% CD45 dim, CD117+, CD34+, CD13+, CD19-, and CD61-myeloblasts. This immunophenotype is consistent with the patient's previous leukemic blasts.

Cyto-Pathology Classification

Immunophenotype

CD45 dim, CD117+, CD34+, CD13+, CD19-, and CD61+/- myeloblasts.

Rearranged Ig Tcr

Not performed.

Pathology

Hypercellular bone marrow (60-70%) with focal sheets of CD34+, CD117+ immature cells.

Electron microscopy

Not performed.

Diagnosis

Hypercellular bone marrow with trilineage hematopoiesis; extensive involvement by acute myeloid leukemia.

Survival

Date of diagnosis: 04-2011

Treatment: History of induction x2; evaluation for initiation of reduced intensity conditioning and/or unrelated stem-cell transplant.

Complete remission : no

Treatment related death : no

Phenotype at relapse

Current disease represents second relapse.

Status: Alive. Last follow up: 10-2011

Survival: 6 months status post second relapse and new chromosome abnormality.

Karyotype

Sample: Bone marrow

Culture time: 24h

Banding: GPW

Results

46,XY,t(8;21)(q22;q22)[5]/46,idem,t(6;22)(p21;q11.2)[3]/46,XY[12]

Karyotype at Relapse

Analysis of bone marrow specimen after 1 additional month of therapy (May 2011) demonstrates the persistence of the 46,XY,t(6;22)(p21;q11.2),t(8;21)(q22;q22) karyotype in 7 out of 20 cells assayed. Morphologic interpretation of this biopsy specimen indicates continued progression of disease.

Other molecular cytogenetics technics

BCR/ABL FISH; AML/ETO FISH.

Other molecular cytogenetics results

200/200 cells assayed negative for BCR rearrangement by FISH. 90/200 cells assayed positive for AML/ETO translocation by FISH.

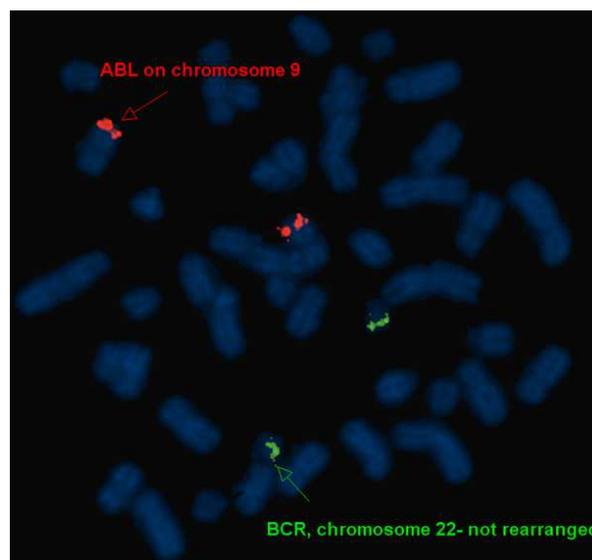
Other Molecular Studies

Technics: Not performed.

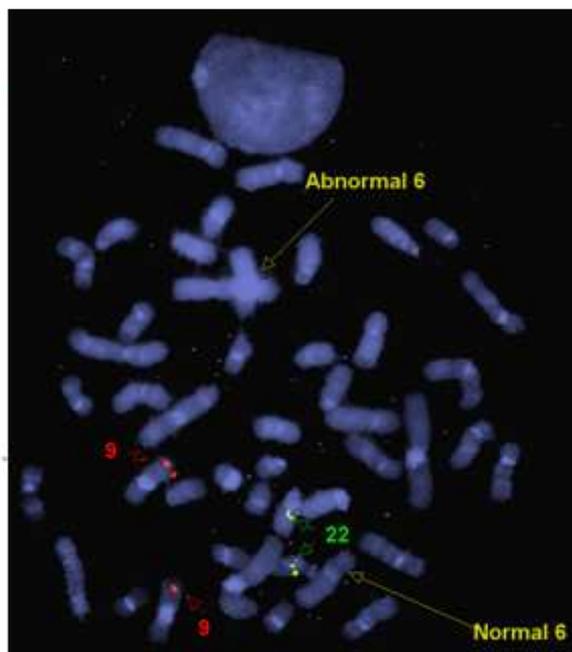
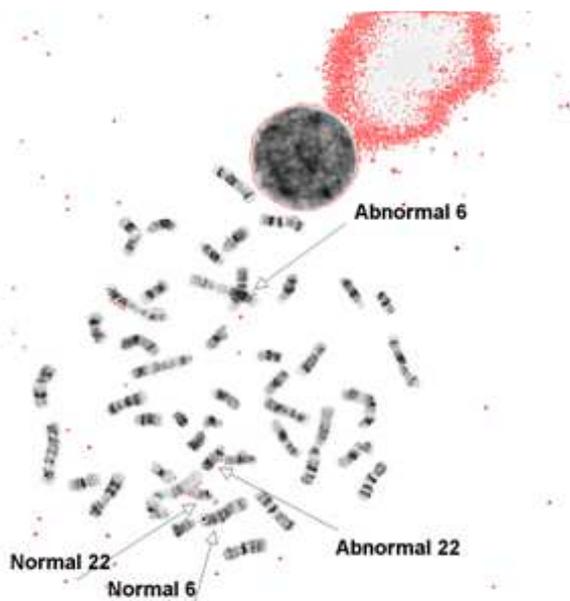
Results: Not performed.



New abnormal karyotype identified in a subset of the patient's relapsed leukemic disease, 46,XY,t(6;22)(p21;q11.2),t(8;21)(q22;q22), present in 3 of 20 cells.



FISH probes for BCR (green) and ABL (red) demonstrating no evidence of a rearrangement involving the BCR locus (22q11.2). All 200 cells assayed from the patient's sample at relapse were negative for BCR rearrangement by FISH.



G-banding (left panel) and FISH (right panel) of the same metaphase spread demonstrating the presence of the BCR locus (green) on chromosome 22 and not chromosome 6.

Comments

Although AML1-ETO t(8;21)(q22;q22) is a well-described cytogenetic anomaly in AML, the t(6;22)(p21;q11.2) seen in this patient's relapse is much more unusual. Few cases have been previously described (Huret, 2010), and only as anecdotal reports in CML, pre-B ALL, and CLL. This is the first reported case of t(6;22)(p21;q11.2) in a patient with AML. Notably, FISH studies targeting the BCR locus (22q11.2) did not reveal evidence of rearrangement, indicating that BCR is not involved in this (6;22) translocation. The appearance of the (6;22) translocation in the background of the patient's previous cytogenetic abnormality indicates clonal evolution of this progressing acute myeloid leukemia.

This pattern of clonal evolution is particularly interesting in light of the patient's somewhat aggressive clinical course, unusual in t(8;21) AML.

References

Huret JL.. t(6;22)(p21;q11). Atlas Genet Cytogenet Oncol Haematol. June 2010. URL : <http://AtlasGeneticsOncology.org/Anomalies/t0622p21q11ID1563.html>.

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