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Case Report Section
Short Communication

JMML evolving to AML in a 14-year-old male acquiring an additional i(X)(q10)

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Abstract

Case report on JMML evolving to AML in a 14-year-old male acquiring an additional i(X)(q10).

Clinics

Age and sex
14 years old male patient.

Previous history
preleukemia The patient is a 14-year-old male who was initially presented at age 12 years 4 month with anemia, leukocytosis, and splenomegaly, when he was diagnosed with juvenile myelomonocytic leukemia (JMML).
Chromosome analysis of bone marrow revealed loss of chromosome 7 (45,XY,-7). The patient achieved complete remission after bone marrow transplantation from a female donor following chemotherapy. At the follow-up visit, 7.5 months after BMT and 10 month after initial visit (AIV), he was found to have 31% blasts in his peripheral blood smear. Bone marrow evaluation was consistent with acute myeloid leukemia (AML) arising out of JMML. Eighteen months AIV the karyotype of 45,XY,-7[9]/45,Y,i(X)(q10),-7[11] was recorded. Chromosome analysis of bone marrow samples 21 and 23 month AIV showed similar karyotypes.
Previous malignancy
No inborn condition of note
No main items

Blood

WBC: 66.2X 10^9/l
HB : 9.7g/dl
Platelets : 42X 10^9/l
Blasts : 31%
Bone marrow: Hypercellular bone marrow (100%), with normal number of megakaryocytes with dyspoiesis, decreased erythropoiesis, increased and left shifted granulopoiesis, and 16% blasts.

Cyto-Pathology Classification

Immunophenotype
JMML leading to AML. Multicolor flow cytometric analysis reveals two abnormal populations: The first abnormal population was 36% large monocytic cells with the following immunophenotype: bright CD11b+, heterogeneous CD13+, CD14+, dim CD15+, heterogeneous CD16+, CD33+, CD36+, CD38+, bright CD45+, bright CD56+, CD64+, partial dim CD71+, CD117+ and heterogeneous HLA-DR+. These cells were negative for CD7 and CD34. CD61 is uniformly positive. It was unclear if this was due to high background staining from platelets versus aberrant expression. The second abnormal population was 4% large myeloid blasts with the following immunophenotype: CD7+, CD11B+, CD33+, CD34+, dim CD45+, CD117+, heterogeneous CD38+, heterogeneous CD56+, partial dim CD71+, and heterogeneous HLA-DR+.

These cells are negative for CD13, CD14, CD15, CD16, CD36, CD61, and CD64. The analysis also identified 7.6% granulocytes.

Pathology
4% atypical myeloid blasts (with expression of CD7,CD11b, heterogeneous CD56, heterogeneous HLA-DR and heterogeneous CD38 and lack of CD13) and an increased population of atypical monocytic cells (36%) (with expression of bright CD56, CD117 and heterogeneous HLA-DR).

Electron microscopy
None

Diagnosis
Acute myeloid leukemia (AML) arising out of juvenile myelomonocytic leukemia (JMML).

Survival

Treatment
Initially patient was diagnosed with JMML. The splenectomy followed by 2 cycles (28 days each) of low dose chemotherapy (consistent of oral mercaptopurine, cis-retinoic acid, low dose cytarabine).
This is followed by allogeneic bone marrow transplant from HLA matched unrelated female donor.
Preparative (conditioning) myeloablative regimen performed with busulfan, fludarabine, antithymocyte globulin (ATG) and graft versus host disease prophylaxis with mycophenolate mofetil and tacrolimus. BMT was performed after 2.5 month AIV and neutrophil engraftment was on day +26 and platelet engraftment on day +24 post-transplant. After BMT the patient received multiple courses of different chemotherapy and immunotherapy in order to achieve remission. Secondary AML arising from JMML was diagnosed after 10 month AIV and standard induction chemotherapy for AML was started (A10D3E5 according to COG-AML1031), due to failure to achieve remission status different agents in different combinations were administered including the following: Azacitadine, oral mercaptopurine, decitabine, lenalidomide, cis-retinoic acid, low dose cytarabine, high-dose cytarabine and mitoxantrone, hydroxyurea. First i(X)(q10) appearance was recorded after 18 month. Eventually the patient underwent a second bone marrow transplant with a different donor 23 month AIV, conditioning with fludarabine and total body irradiation. He is currently awaiting count recovery.
Treatment related death : no

Phenotype at relapse: AML

Status: Alive

Survival: 23months

Karyotype

Sample: BM

Culture time: 24h

Banding: G-banding

Results
45,XY,-7[9]/45,Y,i(X)(q10),-7[11]. Twenty cells were analyzed and two cell lines were detected. Nine (9/20=45%) cells (clone 1) had a modal number of 45 chromosomes, including the X and Y chromosomes.
These cells were missing a chromosome 7 [45,XY,-7]. The remaining eleven (11/20=55%) cells (clone 2) had a modal number of 45 chromosomes, including a Y chromosome, an isochromosome of the long arm of X chromosome, and monosomy 7 [45,Y,i(X)(q10),-7].

Other molecular cytogenetics technics
Fluorescence in situ hybridization (FISH).

Other molecular cytogenetics results
nuc ish(D7Z1,D7S522)x1[285/300]
Fluorescence in situ hybridization (FISH) studies were performed on 300 nuclei using the DNA probes D7S522/CEP 7 [7q31/7cen]. This probe detects the D7S522 deletion [del(7)(q31)] in a fluorescence in situ hybridization dual color assay on cultured cells. The frequency of nuclei with a monosomy 7 signal pattern was 95.0%.

Other Molecular Studies

Technics:
DNA Testing for FLT3 and NPM1 Mutations: PCR.

Results:
FLT3-ITD mutation: Not Detected; FLT3-D835 tyrosine kinase domain mutation: Not Detected; NPM1 exon 12 mutation: Not Detected

Other Findings

Chronic cough, Pancytopenia due to antineoplastic chemotherapy Immunocompromised state, CKD (chronic kidney disease), stage 4 (severe), Bone marrow replaced by transplant, Trachea (stenosis), Nausea, S/P splenectomy, VRE (vancomycin resistant enterococcus) culture positive, Juvenile myelomonocytic leukemia, Palliative care patient, Fluid overload, Acidosis, Uremia, Vitamin D deficiency, Hyperparathyroidism, Hypoalbuminemia, Malnutrition due to renal disease, Hypophosphatemia, Poor appetite, Encounter for antineoplastic chemotherapy, Tracheal stenosis, Chronic renal failure in pediatric patient, stage 5, Tracheitis, Chronic renal failure in pediatric patient (unspecified stage)

Comments

Here we describe a 14 year old male patient who was initially diagnosed with JMML and a bone marrow

karyotype of (45,XY,-7[20]). He developed AML 7.5 month post-BMT. After 18 month AIV the first i(X)(q10) detected. The karyotype of 45,XY,-7[9]/45,Y,i(X)(q10),-7[11] recorded on month 21 AIV. Structural anomalies of X chromosome in hematological malignancies (HM) are uncommon and occur in approximately 1-1.5% of patients (Dewald, GW. et al. 1989, Byrd, JC. et all 2002). The most common anomaly is isodicentric X with idic(X)(q13). The i(X)(p10) and i(X)(q10) are observed less frequently. Most isochromosome X, observed in HM are affecting females. The reported cases in males include i(X)(q10) in a 51-year-old man with common ALL (Bacher, U et al. 2009), a 57-year-old man with Follicular Lymphoma (Donti, E. et al. 1988) and a man with DLBCL of unknown age (Itoyama, T. et al. 2002).

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