**Case Report**

**AML-M2 with der(18)t(1;18)(q2?;p11.3) in addition to t(8;21) and del(9q)**

Sonal R. Bakshi, Shambhu K. Roy, Pina J. Trivedi, Manisha M. Brahmbhatt, Shwetal M. Rawal, Purvi M. Kakadia, Samarth S. Bhatt

Department of Cancer Biology, Cell Biology Division, Division of Research, The Gujarat Cancer Society, The Gujarat Cancer & Research Institute, NCH Campus, Asarwa, Ahmedabad - 380 016, India.

We report a case of Acute Myeloid Leukemia with clinical features suggestive of AML-M3 and 46,XX,t(8;21),del(9q),der(18)t(1;18) karyotype leading to the final diagnosis AML-M2 in light of t(8;21). The Deletion (9q) is a frequent secondary anomaly to the t(8;21)(q22;q22) in AML-M2. In addition to these two AML-M2 related rearrangements we also observed der(18)(1;18)(q2?;p11.3) which may be an unusual rearrangement. This rearrangement resulted into partial trisomy of chromosome #1(q2?) without the loss of any part of chromosome 18, morphologically. Rearrangements of long arm of chromosome 1 that result in complete or partial trisomy for 1q mostly involved the region q25-q32, which may confer a proliferation advantage.

**Key Words:** Acute Myeloid leukemia M-2, Karyotyping, Fluorescence In Situ Hybridization, der(18)t(1;18)(q2?;p11.3),t(8;21),del(9q).

**Introduction**

Total or partial duplication of chromosome 1q and whole arm translocation can result from unbalanced translocation of chromosomes, isochromosomes or jumping translocations. These structural rearrangements are reported as secondary aberrations associated with tumor progression, and advanced disease.¹ Partial duplication of 1q resulting from der(18)t(1;18)(q12;p11) has been reported in Fanconi anemia progressing into myelodysplastic syndrome (MDS).² Translocation of 1q has been reported with telomeres from different chromosome partners: 8pter, 9pter, 12pter, 13pter, 15pter, 17pter, 19pter, 21pter and 22pter.¹

We report partial translocation of 1q to the telomere of 18p resulting into der(18)t(1;18)(1qterà1q2?::18p11.3à18qter) observed as secondary abnormality in a complex karyotype in acute myeloid leukemia (AML-M2). This rearrangement resulted into partial trisomy 1q without any loss of 18p.

**Case History**

A 16 year old female from a low socioeconomic group presented at Gujarat Cancer and Research Institute in November 2000. She had a history of dyspnea, anorexia, low-grade fever, and severe anemia with menorrhagia of 2 months duration. Her CBC revealed; Hb 4 gm%, total WBC count (TC) 16000/mm³, Platelet count (PC) 20,000/mm³ with 60% blasts, 29% polymorphs and 11% lymphocytes. Bone marrow biopsy showed hypercellularity, altered myeloid to erythroid (M:E) ratio, decreased megakaryocytes, mixed erythrocytosis and Sudan black positive. Her bleeding and clotting times were within normal limits. The bone marrow examination revealed; blasts 65%, promyelocytes 61%, myelocytes 02%, metamyelocytes 01%, band cells 01%, polymorphs 19%, eosinophils 4%, lymphocytes 35%, early...
normoblasts 1%, intermediate normoblasts 2%, and late normoblasts 1%. The marrow was hyper-cellular with marked proliferation of atypical blast cells that exhibited round / oval / notched / convoluted nuclei with fine chromatin, and 2-3 nucleoli. There were occasional blasts with Auer rods, many with azurophilic granules, suggestive of acute myeloblastic leukemia with possibility of AML-M2. Plasma fibrinogen level was increased (625 mg% as compared to normal value of 200-400 mg%). The patient was anaemic and thrombocytopenic; hence, multiple fresh frozen plasma, and platelet-rich plasma were transfused. Primolutan-N was given for persistent menorrhagia. She was treated with Daunorubicin 45 mgs/m² for 3 days for 2 cycles from day 6, and All trans-retinoic acid (ATRA) 45 mgs/m² for 26 days in light of the diagnosis of AML-M3 initially, then discontinued due to cytogenetic report of t(8;21) indicating AML-M2. She developed high-grade fever, micturition, neutropenia, and peri-anal abscess. Due to low performance status, further chemotherapy could not be given, and patient was lost to follow-up in June 2001.

Materials and Methods

Short-term culture of bone marrow cells, harvesting and GTG banding was performed according to standard procedures following karyotyping according to ISCN 1995 guidelines. Fluorescence In Situ Hybridization (FISH) using Whole Chromosome Paint probe for #9 (WCP9), and WCP1(Vysis, USA) was performed according to manufacturer’s protocol.

Results

Conventional cytogenetic analysis on G-banded metaphases revealed; 46,XX,t(8;21)(q22;q22),del(9)(q13;q21),add18p(11.3) in all of the 25 metaphases analyzed (Figure 1a and 1b). The additional chromosomal material on one of the 18p seemed to be 1q morphologically. This was confirmed by FISH using WCP1, which showed the presence of chromosome 1 on 18p along with normal #1 pair (Figure 2a) and FISH results for WCP9 excluded cryptic translocation involving #9. (Figure 2b). Moreover, the karyotype showed that there is no monosomy of 18p or part of 18p, morphologically. Thus Cytogenetics led to final diagnosis AML-M2 with complex karyotype.
46,XX,t(8;21)(q22;q22),del(9)(q13;q21),der(18)t(1;18)(q2?;p11.3)3

Discussion

Structural rearrangements of the long arm of chromosome 1 are frequently found in MDS and MPD patients. These changes appear as duplications or translocations with other chromosomes. One situation through which trisomy 1q may arise is widely reported translocation der(1;7)(q10;q10), found particularly in MDS and AML and less frequently in MPD patients.4 Recently two cases of myeloid disorders with der(1;18)(q10;q10) resulting in trisomy 1q and monosomy 18p have been reported. These were proposed to be a novel recurrent unbalanced translocation associated with myeloid disorder.5 Its prognostic significance is not known. A clonal chromosomal abnormality, der(18)t(1;18)(q12;p11) resulting in partial trisomy of 1q with Fanconi’s anemia progressing to MDS has been identified.2 Nevertheless, to the best of our knowledge der(18)t(1;18)(q2?;p11.3) with t(8;21) and del(9q) in AML-M2 as observed in our patient has unusual recurrence.6 It is unbalanced and results in a karyotype in which one normal chromosome 18 is substituted with an intact chromosome 18 with a part of 1q; probably from 1q25 to 1qter region is translocated to the distal end of the band 18p11.3, morphologically. Thus, the rearrangement results in partial trisomy of 1q without the loss of any part of 18p. A complete or partial trisomy for 1q includes the region q25-q32; hence, this region has been postulated to confer a proliferation advantage to the neoplastic clone in a series of patients with hematological malignancy.7 Oncogenes ARG and ABLII were mapped to 1q24-q25, and TRK oncogene was mapped to 1q31.8 Deletion of 9q as a secondary anomaly in t(8;21) is considered to be indicative of worse prognosis, however it is not agreed upon by some workers.9 In the present report, as only one such case is reported and the patient was lost to follow-up, its prognostic significance remains unclear at present.

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