t(3;8)(q26;q24) with *MYC* Rearrangement in Acute Myeloid Leukemia: A Case Report

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Abstract

Rearrangements of 3q26 have been described in 5% of de novo or therapy related acute myeloid leukemia, myelodysplastic syndrome (MDS), and blast phase of chronic myeloid leukemia. The most common translocations involving 3q26 are t(3;12)(q26;p13), t(3;21)(q26;q22), t(3;3)(q21;q26), t(2;3)(p15~23;q26~27) and rarely t(3;7)(q26;q21). However, t(3;8)(q26;q24) with or without monosomy 7 is a rare phenomenon and has been reported in only 10 patients so far. Hereby, we describe a 58 year old patient who was diagnosed with refractory anemia with multilineage dysplasia. Cytogenetic studies revealed monosomy 7. He was then lost to follow-up. A year later he was found to have worsening cytopenias and circulating blasts. He was started on azacytidine. A month later, follow-up bone marrow biopsy showed progression to acute myeloid leukemia (76% blasts). The blasts showed following immunophenotypic profile: CD7+, CD10-, CD13+, CD14-, CD16-, CD33+, CD38+, CD56-, CD64-, CD117-, HLA-DR+, MPO-, cCD3-, cCD22-, cCD79- and TdT-. His karyotype showed evolution with additional finding of t(3;8) which involved *MYC* gene at 8q24 which was confirmed with metaphase FISH. The breakpoint on 3q26 is most likely the *EVI1* fusing with *MYC*. Even though monosomy 7 has been frequently described to be associated with t(3;8), it is not described as a predecessor of t(3;8). Patient failed first induction chemotherapy. He is currently finishing up his re-induction chemotherapy. This case describes a case of AML arising from MDS with monosomy 7 and involving *MYC* gene as a partner for 3q26 (*EVI1*).

Introduction

Ecotropic viral integration site 1 (*EVI1*) gene was first identified in murine myeloid leukemia.[2] *EVI1* was later recognized as a proto-oncogene located on human chromosome 3q26 and associated with the pathogenesis of human acute myeloid leukemia (AML) or myelodysplastic syndrome carrying 3q26 rearrangement. *EVI1* contains 16 exons spanning 64.2 kilobases.[3] It encodes a protein belonging to a family of DNA-binding zinc finger proteins.

Rearrangements of 3q26 have been described in 5% of de novo or therapy related acute myeloid leukemia, myelodysplastic syndrome, and blast phase of chronic myeloid leukemia.[4] The most common translocations involving 3q26 are t(3;12)(q26;p13), t(3;21)(q26;q22), t(3;3)(q21;q26), t(2;3)(p15~23;q26~27) and rarely t(3;7)(q26;q21).[2,3] However, t(3;8)(q26;q24) with or without monosomy 7 is a rare phenomenon and has been reported in only 10 patients so far.

Characteristic features of t(3;8)(q26;q24) are described in previous cases and includes anemia, trilineage dysplasia, megakaryocytic hyperplasia, thrombocytosis.[2] These patients with this specific translocation have poor prognosis.[4,5] Patients with 3q26 rearrangement generally have poor response to therapy.[1]

Case

We describe a 58 year old patient who was diagnosed with refractory anemia with multilineage dysplasia. Cytogenetic studies revealed monosomy 7. He was then lost to follow-up. A year later he was found to have worsening cytopenias and circulating blasts. He was started on azacytidine. A month later, follow-up bone marrow biopsy showed progression to acute myeloid leukemia (76% blasts) (Figure 1). The blasts showed the following immunophenotypic profile: CD7+, CD10-, CD13+, CD14-, CD16-, CD33+, CD38+, CD56-, CD64-, CD117-, HLA-DR+, MPO-, cCD3-, cCD22-, cCD79- and TdT-. His karyotype showed evolution with additional finding of t(3;8) (Figure 2) which involved *MYC* gene at 8q24 which was confirmed with metaphase fluorescence in situ hybridization (FISH) (Figure 3). The breakpoint on 3q26 is most likely the *EVI1* fusing with *MYC*. Even though monosomy 7 has been frequently described to be associated with t(3;8), it is not described as a predecessor of t(3;8). The patient failed two rounds of induction chemotherapy. This case describes a case of AML arising from MDS with monosomy 7 and involving *MYC* gene as a partner for 3q26 (*EVI1*).

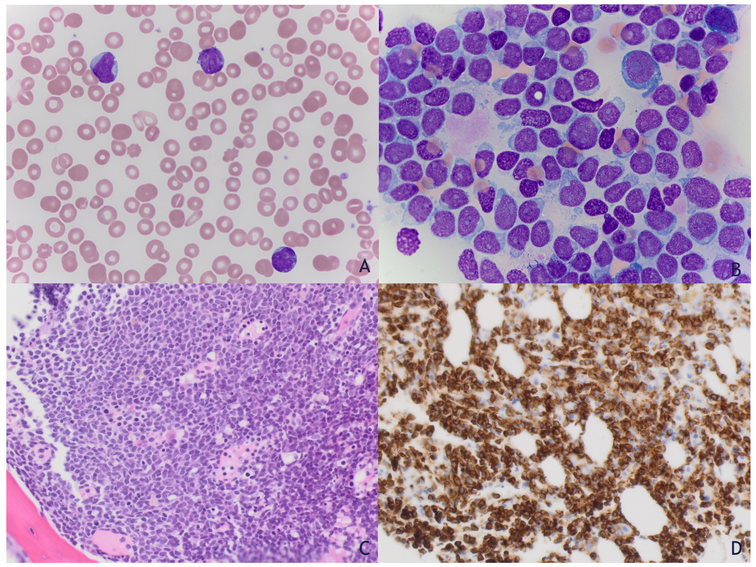

Figure 1: Peripheral blood smear showing circulating blasts (A), Wright-Giemsa stain, 100x oil. Aspirate smear shows sheets of blasts (B), Wright-Giemsa stain, 100x oil. Bone marrow core biopsy shows hypercellular marrow (>95%) with sheets of blasts comprising >90% of total cellularity (C, Hematoxylin and eosin stain, 40x) and immunohistochemical stain for CD34 (D) highlights the blasts, 40x.

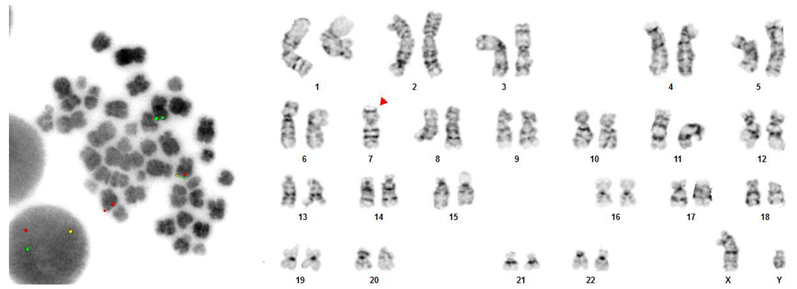

Figure 2: Karyotype shows all 20 GTW banded cells with monosomy 7. Four of these cells also showed an additional material of unknown origin on the long arm of chromosome 8.

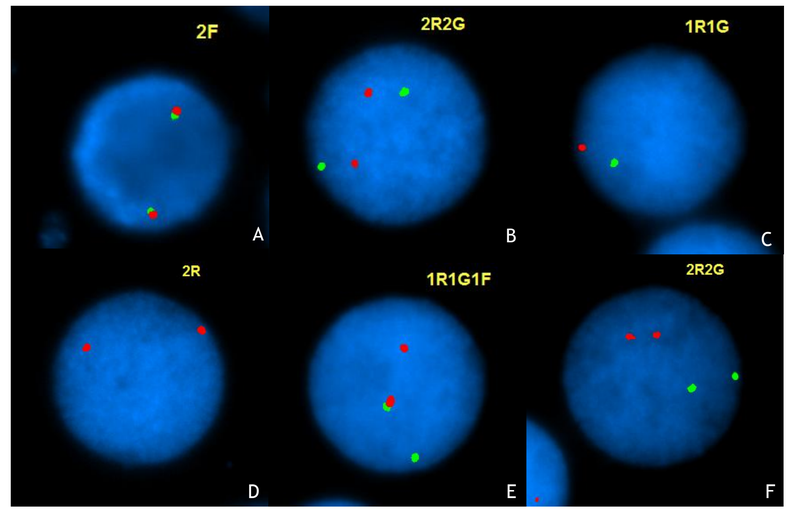

Figure 3: FISH shows monosomy 7 and *MYC* gene rearrangement with 3q. *BCL6* gene rearrangement at 3q27 is negative (A); EGR1/D5S21, D5S23 for -5/5q- is negative (B); D7S522/7 cen for -7/del(7q) is positive in 92.5% of nuclei (C); CEP8 for aneusomy 8 is negative (D); *MYC* for rearrangement of 8q24 is positive in 86.5% of nuclei (E); D20S108 deletion at 20q12 is negative (F).

References

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