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) (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) 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).

Introduction

Ecotropic viral integration site 1 (EVI1) gene was first identified in murine myeloid leukemia.1 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.7 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).7 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 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) 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. Bone marrow core biopsy shows hypercellular bone marrow with 100x oil (B). CD7+ blasts are positive in 86.5% of nuclei (E); D20S108 deletion at 20q12 is negative (F).

Figure 2: Karyotype shows all 26 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 aneuploidy 8 is negative (D); MYC for rearrangement of 8q24 is positive in 86.5% of nuclei (E); D19S108 deletion at 20q12 is negative (F).

References