Letter to the Editor
Diagnostic Hematology

A Novel Case of Extreme Thrombocytosis in Acute Myeloid Leukemia Associated With Isochromosome 17q and Copy Neutral Loss of Heterozygosity

Eunkyoung You, M.D.1,2, Sun Young Cho, M.D.2, John Jeongseok Yang, M.D.2, Hee Joo Lee, M.D.2, Woo-In Lee, M.D.2, Juhiee Lee, M.D.3, Kyung Sam Cho, M.D.4, Eun Hae Cho, M.D.5, and Tae Sung Park, M.D.2

Department of Medicine1, Graduate School, Kyung Hee University, Seoul; Departments of Laboratory Medicine2, Pathology3, and Hematology-Oncology4, School of Medicine, Kyung Hee University, Seoul; Green Cross Genome5, Yongin, Korea

Dear Editor
An isochromosome of the long arm of chromosome 17, i(17q), has been frequently reported in the blast phase of CML [1], and is also associated with various types of hematological diseases [2]. While it is believed that i(17q) as a sole abnormality is a distinctive clinicopathological entity with a high risk of leukemic progression, a subset may be present as de novo AML [3].

Extreme thrombocytosis is rare in AML, and only a few cases have been described with chromosome 3 abnormalities [4, 5]. In addition, the loss of heterozygosity (LOH) affecting chromosome 7q is common in AML and MDS, suggesting the essential role of this region in disease phenotypes and in clonal evolution. Presented here is a case of AML with myelodysplasia-related changes (AML-MRC) with extreme thrombocytosis, 7q LOH, and i(17q).

A 76-yr-old Korean male was referred for thrombocytosis. The initial complete blood count (CBC) showed a Hb level of 8.9 g/dL, a platelet count of 1,746×10^9/L, and a white blood cell (WBC) count of 14.65×10^9/L with 43% blasts (Fig. 1A). The dysplastic features observed on a peripheral blood smear were marked anisocytosis of red blood cells (RBCs), pseudo-Pelger-Huet-like neutrophils, and extreme thrombocytosis with giant and large platelets (Fig. 1B). Bone marrow aspiration smears displayed hardly visible hematopoietic components owing to extreme thrombocytosis and dyspoietic megakaryocytes (Fig. 1C). Micro-megakaryocytes with the dyspoietic features of binucleation or non-lobulated shapes were observed (Fig. 1D). From visible fields located at the periphery of aspiration slides, 37.8% of leukemic blasts were seen. Focal fibrosis of the bone marrow was observed from the biopsy section. The results of BCR-ABL1, JAK2 V617F, MPL W515L/K, and CALR exon 9 mutation tests were all negative. Immunophenotyping revealed that the blasts were positive for CD34, CD13, HLA-DR (moderate), CD33, and CD38 (dim), which was consistent with AML. The chromosome study showed a karyotype of 46,XY,i(17)(q10) in 18 out of 20 metaphase cells (Fig. 2A). The patient was diagnosed as having AML-MRC.

A high-resolution microarray analysis using a cytogenetics whole genome 2.7M array (Affymetrix, Santa Clara, CA, USA) was conducted after obtaining informed consent for further analysis. The microarray analysis also revealed abnormalities of chromosome 17, which was consistent with the conventional cytoge-
Germ-line findings; the abnormalities were represented as arr 17p13.3p11.2(64,214-18,751,820)×1,17p11.2q25.3
(18,751,820-80,587,411)×3 (Fig. 2B). Incidentally, the micro-
array analysis also detected a copy neutral LOH as arr7q11
.1q36(59,000,001-159,138,663)×2 homozygous (hmz) (Fig.
2C). After being diagnosed as having AML-MRC, the patient re-
fused to continue with chemotherapy and expired 10 months af-
ler diagnosis.

According to the study by Rashmi et al. [3], most cases of my-
eloid neoplasm with i(17q) show anemia, leukocytosis, thrombo-
cytopenia, and splenomegaly. Morphologically, all cases show
features of both myelodysplasia and myeloproliferation (pseudo-
Pelger-Huet-like neutrophils, micromegakaryocytic hyperplasia,
hypercellularity, fibrosis, and osteosclerosis) [3]. It has been sug-
gested that granulocyte colony-stimulating factor and myeloper-
oxidase positioned at 17q21.1 and 17q23.1, respectively [6, 7],
are responsible for myeloproliferative features in the presence of
i(17q), where duplication of 17q occurs [3, 8]. In our case, most
of the features were consistent with characteristic findings of my-
eloid neoplasms with i(17q). However, extreme thrombocytosis
was a characteristic feature that differed from the previous re-
port, which reported mostly thrombocytopenia [3].

Marked thrombocytosis is rarely associated with AML, and
thrombocytosis with a platelet count over 1.0×10^12/L is an ex-
Extremely rare phenomenon, even for a patient with chromosome 3 abnormalities [4]. Our patient had a platelet count of 1,746 x 10^9/L at diagnosis, but no abnormalities of chromosome 3 were found. To our knowledge, this is the first reported case of marked thrombocytosis with AML associated with i(17q) and not with chromosome 3.

During further investigation of i(17q) using a single nucleotide polymorphism array (SNP-A), copy neutral LOH 7q was incidentally detected. LOH 7q is common in AML and MDS and seems to play an important role in the phenotype and characteristics of these diseases [9]. A recent study by Jerez et al. [9] found a correlation between the presence of LOH 7q and diploid MDS/MPN. However, no AML-MRC cases had extreme thrombocytosis.

Our case showed features that were consistent with i(17q) in myeloid neoplasms; most of the morphological and clinical features of our patient could be explained as characteristic features of i(17q). However, the finding of marked thrombocytosis and 7q LOH, seemed rather irrelevant and unrelated. A close follow-up of such unusual cases could provide further clinical information on AML-MRC with extreme thrombocytosis accompanied by i(17q) and 7q LOH, while additional studies are necessary to delineate and characterize the development of such unique cases.

Authors’ Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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