

A Tandem Triplication Of Chromosome 1q As Second Karyotypic Aberration In A Patient With Acute Myelogenous Leukemia

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Abstract

Triplication of the long arm of chromosome 1 (trp(1q)) is a very rare karyotypic abnormality in hematologic diseases. We report a case of acute myelogenous leukemia whose karyotype carried trp(1q) that was proved to be addition to preceding trisomy 8.

A 62 year-old woman who visited our department because of general fatigue presented pancytopenia. Bone marrow examination revealed hypocellularity containing 22.4% of blastic cells. Acute myeloid leukemia with maturation was diagnosed. Karyotypic analysis of her marrow leukemic cells showed 47,XX, trp(1)(q21;q32),+8 in 19 of the 20 metaphases and 47,XX,+8 in the remaining one. Remission induction failure and combination chemotherapy had been repeated for the disease control. She died of interstitial pneumonia 3 years after the initial presentation.

To date, trp(1q) has been shown to be involved in the pathogenesis of leukemia, myelodysplastic syndrome, lymphoma, and so on. However, the frequency is too low to elucidate precise role. Thus, world-wide accumulation of clinical data of trp(1q) is required.

INTRODUCTION

Triplication of the long arm of chromosome 1 (trp(1q)) is a very rare karyotypic abnormality first reported by Papenhausen et al. in a patient with myelodysplastic syndrome (MDS)[1]. To date, this abnormality has seldom been described and is usually a part of complex karyotypic aberrations[2]. Although it has also been detected as a sole abnormality in hematologic diseases (acute myelogenous leukemia[3], myelodysplastic syndrome[4], myeloficrosis[5] and Fanconi anemia[6]), its role in the pathogenesis is not elucidated.

It is well known that karyotype of malignancies often evolves during the progression of the disease. Particularly, karyotypic evolution in leukemic transformation of MDS has precisely been analyzed[7]. We report a case of acute myelogenous leukemia whose karyotype carried trp(1q) that was proved to be addition to preceding trisomy 8.

CASE PRESENTATION

62 year-old woman visited our department because of general fatigue that had developed within a month. Complete blood count revealed pancytopenia with white blood cell of $2.34 \times 10^9/L$ with 2% of blastic cells, red blood cell of $2.1 \times 10^9/L$, hemoglobin level of 7.2g/dL, and platelet of $29 \times 10^9/L$ and bone marrow was examined immediately. Hypoplastic marrow with nucleated cell count of $2.1 \times 10^9/L$ containing 22.4% of blastic cells was observed. The blasts contained multiple azurophilic granules, indicating a tendency of maturation. Morphological dysplasia such as hypolobular neutrophils and erythroblasts with basophilic stippling was apparent, but the frequency was too low to be sufficient for the criteria of myelodysplasia-related changes. Serum LDH was elevated at 254IU/L. Acute myeloid leukemia with maturation according to WHO classification[8] was diagnosed. Leukemic cells showed positivity for CD13, 15, 64, 65, 71, 117, and HLA-DR by flowcytometry.

Karyotypic analysis of her marrow leukemic cells was carried out as described[9]. Among 20 metaphases analyzed, trp(1)(q21;q32) accompanied by trisomy 8 was observed in 19 cells, and solely seen trisomy 8 in the remaining one (Figure).

Idarubicin and cytarabine were administered as remission induction. Although leukemic cells in her marrow decreased to 2% of nucleated cells, those cells resided in peripheral blood, indicating induction failure. To reduce leukemic cell expansion, combination chemotherapy with various anthracycline agents and cytarabine was repeated approximately once in a few months. Karyotypic evolution was observed after one year from the initiation of chemotherapy. It was shown that all 20 metaphases carried 47,XX, trp(1)(q21;q32),+8. A metaphase with +8 as a sole abnormality was not detected. She suffered from interstitial pneumonia 3 years after the presentation, and died of it despite administration of antibiotics, antifungal agents, and antiviral agent.

Figure 1a

Triplication of chromosome 1q between band q21 and q32 is seen with trisomy 8 in 19 metaphases.

Figure 1b

Only trisomy 8 is detected in the remaining one metaphase, indicating that this is primary karyotypic change followed by triplication of 1q.

DISCUSSION

When trp(1q) is detected as sole abnormality in neoplastic cells, its role in the pathogenesis appears to be critical. Actually, Ha et al. showed a genomic gain on the triplicated segment between chromosome 1q21 and q32 using comparative genomic hybridization in a patient with refractory cytopenia with multilineage dysplasia[4]. Since genomic imbalance was not observed in other chromosomal regions, this gain plays a genetically important role for the genesis of myelodysplasia.

Although sequential karyotype analysis has rarely reported in patients carrying trp(1q), trp(1q) has been considered as early chromosomal change[4]. Actually, Papenhausen et al. presented karyotypic evolution from sole trp(1q) to additional trisomy 8[1]. Of interest, our patient showed the inverse evolution of karyotype; The initial karyotype was supposed to be 47,XX,+8 as found in a single metaphase, and the evolved one 47,idem, trp(1)(q21;q32) in 19 metaphases. It might be supposed that trisomy 8 in this case contributed to the development of preceded MDS and

trp(1q) is responsible for the leukemic change. The identical karyotype was also described by Cho et al. in a patient with refractory anemia with excess of blasts[10]. Trp(1q) and trisomy 8 might cooperatively cause leukemia regardless of an order to appear.

Since duplication of chromosome 1q was reported to be associated with leukemic transformation of MDS, resulting in poor prognosis[11], trp(1q) was also considered to have similar significance on the prognosis. However, our patient was alive for 3 years despite refractoriness to induction chemotherapy. Patient who was described by Papenhausen et al. lived for at least 6 years[1]. Prognostic significance of trp(1q) is thus still debatable. Because of the extremely low frequency, world-wide accumulation of clinical data and genetic analysis of trp(1q) are needed to elucidate the role in the tumorigenesis.

References

- 1) Papenhausen PR, Wolkin-Friedman E, Pekzar-Wissner C. Novel tandem triplication of 1q in a patient with a myelodysplastic syndrome. *Cancer Genet Cytogenet* 1984; 12: 145-150.
- 2) Park TS, Lee ST, Song J, Lee KA, Kim J, Kim SJ, Lee JH, Song S, Choi JR. A tandem triplication, trp(1)(q21;q32), in a patient with follicular lymphoma: a case study and review of the literature. *Cancer Genet Cytogenet* 2009; 189: 127-131.
- 3) Tien HF, Wang CH, Chuang SM, Chow JM, Lee FY, Liu MC, Chen YC, Shen MC, Lin DT, Lin KH. Cytogenetic studies, ras mutation, and clinical characteristics in primary myelodysplastic syndrome: a study on 68 Chinese patients in Taiwan. *Cancer Genet Cytogenet* 1994; 74: 40-49.
- 4) Ha JS, Choi MS. 1q triplication as sole cytogenetic abnormality in myelodysplastic syndrome. *Leuk Lymphom* 2011; 52: 1387-1389.
- 5) Park TS, Lee SG, Cheong JW, Song J, Lee KA, Kim J, Yoon S, Choi JR. Two case reports of 1q triplication in myeloproliferative neoplasms. *Cancer Genet Cytogenet* 2009; 191: 111-112.
- 6) Ferro MT, Vazquez-Mazariego Y, Ramiro S, Sanchez-Hombre MC, Villalon C, Garcia-Sagredo JM, Ulibarrena C, Sastre JL, Roman CS. Triplication of 1q in Fanconi anemia. *Cancer Genet Cytogenet* 2001; 127: 38-41.
- 7) Horiike S, Taniwaki M, Misawa S, Abe T. Chromosome abnormalities and karyotypic evolution in 83 patients with myelodysplastic syndrome and predictive value for prognosis. *Cancer* 1988; 62: 1129-1138.
- 8) Arber DA, Brunning RD, Orazi A, Porvit A, Peterson L, Thiele J, Le Beau MM. Acute myeloid leukaemia, not otherwise specified. In: Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J, Vardiman JW, editors. *World Health Organization Classification of tumours of haematopoietic and lymphoid tissue*. 4th ed. IARC Press: Lyon; 2008: p. 130-139.
- 9) Misawa S, Horiike S, Taniwaki M, Abe T, Takino T. Prefixation treatment with ethidium bromide for high resolution banding of chromosomes from cultured human bone marrow cells. *Cancer Genet Cytogenet* 1986; 22: 319-29.

10) Cho HS, Kim MK, Hyun MS. Triplication of 1q in a patient with myelodysplastic syndrome. Korean J Hematol 2006; 41: 56-60.

11) Alfaro R, Perez-Granero A, Duran MA, Besalduch J,

Rosell J, Bernues M. dup(1)(q21q32) as a sole cytogenetic event is associated to a leukemic transformation in myelodysplastic syndromes. Leukemia Res 2008; 32: 159-161

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