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Gain of an Isochromosome 5p: a Rare Recurrent Abnormality in Acute Myeloid Leukemia

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Abstract. *Chromosomal abnormalities characterize the biological behavior of acute myeloid leukemia (AML), also facilitating the identification of genes responsible for its development and/or progression. Isochromosome 5p, i(5p), represents a rare chromosomal abnormality described, to date, in only a few AML cases. In almost all the cases reported, the i(5p) was accompanied by other abnormalities. Here, a new case of AML, evolved from a myelodysplastic syndrome (MDS) with a clonal trisomy 8, is reported. The case presented the following karyotype: 46,XY[15]/47,XY,+8[4]/47,XY,+i(5)(p10)[3]/48,XY,+i(5)(p10)+8[3]. To our knowledge, this is the first reported case of AML to present a clone with an isolated i(5p). The cytogenetic findings supported the hypothesis that i(5p) may represent a primary abnormality, which characterizes a small subset of AML cases.*

Acute myeloid leukemia (AML) is a heterogeneous disease in terms of both its biology and clinical outcome. Chromosomal abnormalities characterize the biological behavior of acute leukemias and also point to relevant genes for disease development or/and progression. Isochromosome 5p, i(5p), represents a rare chromosomal abnormality described, to date, in only a few AML cases. In almost all the reported cases, the i(5p) was accompanied by other abnormalities, especially trisomy 8 (1-3). In the present study, of 59 cytogenetically abnormal cases of AML analyzed in our laboratory, an i(5p) was found in only one case.

Materials and Methods / Results

On reviewing cases of AML cytogenetically studied in our laboratory, 59 cases with an abnormal karyotype were found. All the cases were studied by direct culture of bone marrow cells and a G-banding technique. As many cells as possible were analyzed in each case, and not fewer than 20. An abnormal clone was defined as two or more metaphases with either the same structural anomaly or the same extra chromosome, or as three or more metaphases lacking the same chromosome. The karyotypes were described according to the International System of Human Cytogenetic Nomenclature (ISCN 1995) recommendations (4). Among all the 59 cytogenetically abnormal cases, an i(5p) was found in only one case of myelomonocytic leukemia, the M4 French-American-British (FAB) subtype (5), evolved from a myelodysplasia syndrome (MDS) with a known clonal single trisomy 8 (Figure 1). Further clinical data were not available for this case. Two unrelated clones with either an i(5p) or trisomy 8 were found, while a third clone had both i(5p) and trisomy 8. Thus, the case presented the following karyotype: 46,XY[15]/47,XY,+8[4]/47,XY,+i(5)(p10)[3]/ 48,XY,+i(5)(p10)+8[3].

Discussion

Chromosomal abnormalities are found in about 40-45% of AML cases. These abnormalities include balanced chromosomal aberrations as the primary abnormality and unbalanced karyotypic abnormalities without a primary balanced aberration. Balanced aberrations lead to the generation of leukemic-specific fusion genes, most of which have been analyzed in detail at the molecular level, while they have also been shown to be implicated in the pathogenesis of AML. In contrast, the pathogenetic role of unbalanced abnormalities has not yet been defined. Notably, close correlations between cytogenetic abnormalities and certain morphological characteristics of AML have been found. The identification of chromosomal abnormalities in AML is of major clinical importance, facilitating the establishment of the exact diagnosis, predicting prognosis and monitoring therapy strategies (1).

An i(5p) has been reported in only a few cases of AML. In the present study, among 59 cytogenetically abnormal AML cases, an i(5p) was found in one case FAB-M4 subtype evolved from a MDS with a known clonal single trisomy 8.

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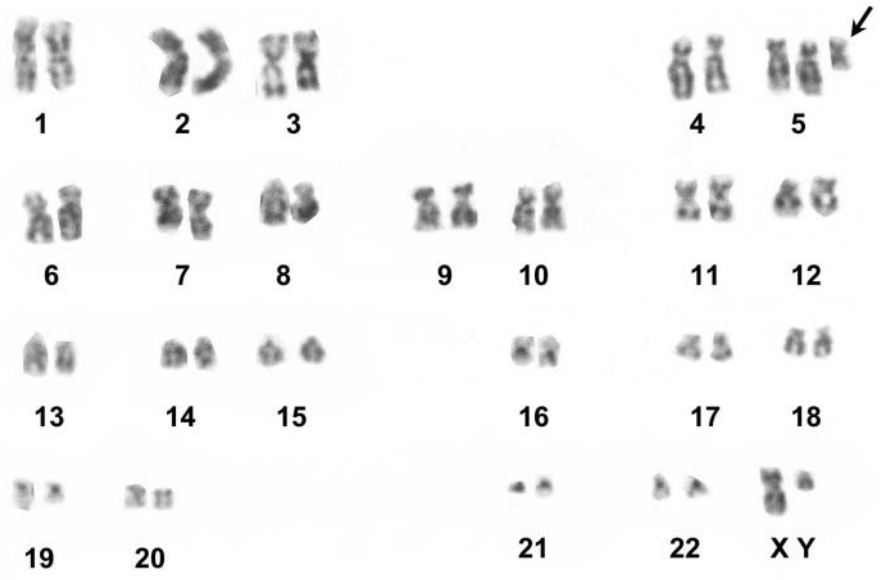

Figure 1. *Karyotype of a metaphase showing i(5p).*

Apart from the clonal trisomy 8, the case presented two additional abnormal clones, one with an isolated i(5p) and the other with both trisomy 8 and i(5p). Schoch *et al.* (3) presented three cases of acute monoblastic leukemia with both an i(5p) and trisomy 8. On reviewing the literature, they found two additional cases of AML of M2 and M4 FAB-subtype, respectively, with an i(5p) and complex chromosomal abnormalities (6, 7). The authors reported that all these five patients showed a poor response to chemotherapy. Because of the high incidence of trisomy 8 as the sole anomaly in the monocytic leukemia and the presence of trisomy 8 in four of these cases with monocytic lineage involvement, the authors supported the hypothesis that i(5p) might represent a secondary change. Our literature review identified two additional cases of AML M5 FAB-subtype with an i(5p) and complex karyotypes (2, 8, 9). One of them also presented trisomy 8. To our knowledge, the case described here is the first reported in the literature to present a clone with an isolated i(5p). Unfortunately, clinical data are not available for the case. However, the cytogenetic findings may support the hypothesis that i(5p) represents a primary change implicated in the initiation or progression of the neoplastic process in a small subset of AML cases.

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