The common translocation responsible for leukemogenicity in acute promyelocytic leukemia (APL) is the reciprocal translocation of chromosome 15 to chromosome 17. We present an unusual case of APL with structurally normal chromosomes 15:17 and triploid and tetraploid clones found in the karyotype of bone marrow cells.

The cytogenetic hallmark in 95% of cases of acute promyelocytic leukemia (APL) is a balanced reciprocal translocation between the long arms of chromosome 15 and 17. The cytogenetic abnormality in rare cases involves reciprocal translocations of chromosomes 5, 6, 11, 13, 8, 7 or 19 to chromosome 17. The molecular defect in APL was found to be the disruption of the α-receptor of retinoic acid (RARα) and its reciprocal, in frame fusion, with one of four partner genes (transcription factors) namely: PML, located in chromosome 15, PLZF and NuMA in chromosome 11 and NPM in chromosome 5.

We report a case of APL with impressive blast morphology and unusual cytogenetic findings: triploid and tetraploid clones were detected in the patient’s bone marrow cells. To our knowledge, polyploidy has never been previously reported in APL. A 49-year old male presented for evaluation because of leukopenia, anaemia and mild thrombocytopenia, during the last trimester of 1998. He was fairly asymptomatic without any abnormal physical signs. His medical history was unrevealing. Laboratory tests showed Hb: 12.3 g/dL, white blood cell count 12×10^9/L with differential count: neutrophils 42% with dysplastic features, 46% lymphocytes and 12% monocytes and platelets 113×10^9/L. Biochemical blood tests were within normal limits, except for a slightly elevated lactic dehydrogenase (268 IU - upper normal limit 240 IU) and a low fibrinogen (109-80 ng/mL). Coagulation tests were within the normal range.

Bone marrow aspiration and biopsy revealed bone marrow infiltration by large blasts with eccentric nucleus, without prominent nucleoli and abundant, hypergranular cytoplasm comprising 72% of the cell population. Ten percent of the leukemic cells had an easily visible network of Auer rods, or bundles (Figure 1a). The granulocytic, erythrocytic and megacaryocytic cell lines were depressed. Leukemic cells stained strongly for myeloperoxidase in histochemistry. The immunophenotype of leukemic cells was: CD3=11%, CD5=11%, CD11β=3%, CD11c=2%, CD19=34%, CD10=21%, CD20=4%, CD33=69%, CD38=67.4%, HLA-DR=5.2%, CD56=10.3%, CD13=61%, CD45=87.6%.

Cytogenetic analysis of bone marrow cells was carried out twice. The first analysis revealed the presence of a tetraploid clone. Nine of 22 examined metaphases had the karyotype 92 XXY. A second karyotype analysis of 33 cells, performed 28 days later, revealed 11 normal diploid metaphases, (Figure 1b) 4 triploid and 18 tetraploid metaphases. There was no evidence of structural rearrangements (15:17) included (Figure 2). Molecular analysis of bone marrow blast cells with reverse transcription polymerase chain reaction showed a PML/RARα fusion gene transcript of the bcr3 type. No structural alterations were detected in either the diploid or polyploid metaphase cells. Fluorescence in situ hybridization experiments could not be carried out at diagnosis to exclude cryptic translocations other than PML/RARα.

Our case is the first report of polyploidy in APL with the presence of the PML/RARα transcript. No structural alterations were detected in either the diploid or polyploid metaphase cells. Fluorescence in situ hybridization experiments could not be carried out at diagnosis to exclude cryptic translocations other than PML/RARα.

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In a detailed review of various translocations that have been described in acute promyelocytic leukemia, Cognieli et al., refer to many kinds of translocations either carrying or not the different chimeric transcripts.

In our case, the detected hybrid fusion product PML/RARα

description of M 3 type of acute leukemia with regular nuclei, hypergranular cytoplasm, Auer rods forming occasionally bundles, and a low percentage of CD56 positive cells in the immunophenotype.1

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comprises the essential component of APL leukemogenesis. Hiorns et al. have described an APL case with PML/RARα typical fusion gene bearing intact chromosomes 15 and 17 and

t15q22p13q12. In our patient, chromosome 15 was among the 18 tetraploid metaphases and interestingly chromosome 17 was included in triploid metaphases. The treatment outcome in our patient was favorable, as would be expected in PML/RARα positive APL.1,5,6

It is possible that in our case genetic instability was combined with factors favoring excessive DNA replication. Hybrid genes responsible for growth or programmed cell death, such as PML/RARα and the repression complex, induced block of differentiation and at the same time other transcription factors were involved in errors of aberrant DNA replication.3 Possibly this dysregulation of transcription factors generated triploid or tetraploid metaphases in the leukemic clone.

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Key words: cytogenetics, triploidy, tetraploidy, atypical APL.

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