Case report

Two copies of isochromosome 5p in refractory cytopenia with multilineage dysplasia: A case report

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1. Introduction

Loss of material from chromosome arm 5q is a common abnormality in myelodysplastic syndrome (MDS) and, if it is the only one, it’s recognized as a distinct pathological entity (“isolated 5q- syndrome”) with good prognosis.

In contrast, gain of material from chromosome 5 is a rare event; the formation of an isochromosome of the short arm – i(5)(p10) – has been described in a very few cases of MDS and in about ten patients with acute myeloid leukemia (AML). The formation of i(5)(p10) results from the loss of the long arm of chromosome 5 and duplication of its short arm.

In literature, two types of i(5)(p10) are observed 1:

1) i(5)(p10) inducing a loss of the long arm of the chromosome (monosomy 5q and trisomy of the short arm)

2) a supernumerary i(5)(p10), in addition to two normal chromosomal 5, resulting in a tetrasomy of the short arm.

Here we report a MDS case with two copies of isochromosome 5p and a single normal chromosome 5. To our knowledge, the pentasomia 5p has never been described before the present study.

2. Materials and methods

2.1. Patient

In 2008, a 69-year-old man, who presented isolated thrombocytopenia without immunological basis for several years (Hb 13.6 g/dL; WBC 8.9 x 10^3/mm^3; PLT 49.0 x 10^3/mm^3), was submitted to bone marrow aspiration. Diagnosis was consistent with myelodysplastic syndrome: sample showed erythrocytic hyperplasia with dyserythropoiesis and a normal number of megakaryocytes, mostly of small size.

In June 2012, the patient, in addition to chronic thrombocytopenia, developed invertebrate anemia (HB 8.3 g/dL). A new cytomorphic analysis of bone marrow aspiration was
performed and confirmed dysplastic features. A bone marrow biopsy allowed classification as "refractory cytopenia with multiligneage dysplasia" (RCMD), without excess of blasts (WHO 2008); no peculiar morphophtotypical feature was observed.

In September 2012, his clinical conditions worsened dramatically, with these parameters of pancytopenia: Hb 5.3 g/dL; WBC 1,990/mm³; PLT 8,000/mm³.

2.2. Cytogenetic study

In June 2012, cytogenetic studies were performed on unstimulated peripheral blood and bone marrow cells, after 24 and 48 h cultures.

Chromosomes were identified using standard Q-banding techniques and the karyotype was described according to the International System of Human Cytogenetic Nomenclature (ISCN 2009).

2.3. FISH

The isochromosomes 5p were confirmed by fluorescence in situ hybridization (FISH) using a specific probe for 5p15 labeled with FITC; a probe for EGR1 locus on 5q31 labeled with Texas Red was co-hybridized (Cytocell, Cambridge, UK).

3. Results

Thirty metaphases from bone marrow cultures were studied and the karyotype was 47,XY,i(5)(p10),+i(5)(p10),t(7;10)(q35,q32)[12]/47,XY,i(5)(p10),+i(5)(p10)[8]/46,XY[10].

In summary, the analysis revealed only one normal chromosome 5 and two copies of isochromosome 5p, resulting in a pentasomia 5p and monosomia 5q. An additional aberration was associated in 12/20 abnormal metaphases: an apparently balanced translocation between long arms of chromosomes 7 and 10. Derivative chromosome 7 was confirmed by FISH.

Peripheral blood cell analysis showed only few metaphases and the same clonal abnormalities were found.

4. Discussion

To date, an i(5)(p10) has been found in a very small number of patients (10 AML, 4 MDS, one secondary MDS after treatment of a multiple myeloma). In particular, among MDS patients there were one case of refractory cytopenia with multilineage dysplasia and another one of refractory anemia with ringed sideroblasts.

In all published cases, the i(5)(p10) was present in single copy and accompanied by one or more additional anomalies, mostly trisomy 8. The biological and clinical significance is yet unclear, not only because too few cases have been described, but also because these aberrations usually occur within a complex karyotype, in itself with poor prognosis.

To our knowledge, this is the first reported case of hematological disorder to show clones with two copies of i(5)(p10).

Though our patient received a diagnosis of MDS in 2008, he remained without any treatment, but for a periodical administration of prednisone due to thrombocytopenia. In addition, he has recently developed severe pancytopenia and he needs blood transfusions.

Unfortunately, no cytogenetic analysis was performed at the onset of disease; therefore we cannot establish whether the i(5)(p10) aberration represents a driving change or rather a progression event.

Interestingly, our patient is affected by inherited hemochromatosis (compound heterozygote H63D/C282Y), genetic defect leading to uncontrolled iron deposition, mostly in parenchymal organs. Recent studies have displayed a non random relationship between C282Y and H63D mutations of hemochromatosis gene and myelodysplasia, suggesting a possible role of iron overload in pathogenesis of myelodysplastic disorders.

The common transfusion-dependence of MDS patients may also contribute to increase hemosiderosis, as in a vicious circle, and an early administration of iron-chelating agents should be taken in consideration.

In agreement with former studies, we emphasize the relevance of using specific probes of chromosome 5p/5q as a necessary complement of conventional karyotype, because an isochromosome 5p may lead to a wrong conclusion of metacentric del(5q), a much more common finding.

In conclusion, i(5)(p10) is a rare but recurrent abnormality in myeloid disorders, especially in AML. Although the bone marrow biopsy of our patient didn’t show excess of blasts, cytogenetic findings of two copies of isochromosomes 5p and an additional translocation deserve a close follow up.
In fact his pancytopenia is increasing quickly.

**Conflict of interest statement**

None.

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**References**