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Case report

Association of a deletion 5q- and a translocation t(2;11) in a case of refractory anaemia

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Abstract. This paper presents a clinical case with myelodysplasia (refractory anaemia) and 5q- syndrome which shows an unusual additional cytogenetic abnormality [deletion 5q- associated with a t(2;11)]. Fourteen cases have been reported until now in the literature and this is the first case described in Algeria. In addition to this case description; an up to date pathogenic approach is discussed in accordance to new molecular knowledge of myelodysplasia biology.

Key words: refractory anemia • 5q- syndrome • translocation (2;11)

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INTRODUCTION

The myelodysplastic syndromes (MDS) represent a heterogeneous group of clonal haematopoietic cell disorders having a maturation arrest and resulting in peripheral blood cytopenia. MDS have a common denominator; they end up to an acute myeloblastic leukaemia, which occurs in a quarter to a third of the cases[1]. Cytogenetic abnormalities are observed in 30 to 50% of MDS cases[2], having not only diagnostic but prognostic value as well. They also help to identify the genes implicated in the MDS pathogenesis. In this particular case, the translocation t(2;11) is a relatively rare event and only fourteen cases have been described in the literature. At the university hospital of Oran among 39 MDS patients[3] we have observed a new case with this translocation together with a 5q deletion[4].

CASE REPORT

A 56 year-old man, was consulted in May 1996 for fatigue, weakness and mucocutaneous pallor, installed progressively. His medical history included hypertriglyceridaemia only. On admission, clinical examination revealed a conscientious patient in a good performance statue (PS1), weakness, exertion dyspnoea, and vertigo. There was no thoracic pain, his blood pressure was 120/70 mm Hg, and the pulse rate was 84/min. There were no lymphadenopathy, splenomegaly or hepatomegaly.

His haematological profile was as follows: WBC $5x10^9$/l, neutrophils $2,8x10^9$/l, lymphocytes $1,3x10^9$/l, haemoglobin 7g/dl, MCV 110fl, platelet $266x10^9$/l. The bone morrow aspiration showed an hypercellular marrow with a decreased percentage of the erythroid elements, mononuclear micromegakaryocytes, without any blast excess. Serum ferritin was slightly in-

creased. The iron staining of the bone marrow aspirate did not show any ring sideroblasts. Patient's blood group was A Rh^+. The HBV, HCV, HIV serology was negative. Karyotypic analysis revealed the cytogenetic abnormalities (5q-associated to translocation t(2;11)). The diagnosis of MDS (refractory anaemia) was established by the characteristic karyotypic abnormality.

The patient was treated firstly with androgens (Danasole®), then with corticosteroids and red blood cells transfusion, with no effect. Finally we decided to use red blood cells transfusions alone as needed, using an iron chelator for preventing iron overload (Deferral®).

DISCUSSION

In MDS the t(2;11) translocation is a rare event; only fourteen cases have been described in the literature. Talman et al has described 8 patients with this karyotypic abnormality: 5 had refractory anaemia, 1 refractory anaemia with ringed sideroblasts and 2 acute myeloblastic leukaemia[5].

The review of the literature showed that 6 cases had an isolated t(2;11) abnormality, while 8 cases had a t(2;11) translocation together with other karyotypic disorders; del(5q-) being the most frequent (6 cases). We report here another case with the combination of t(2;11) and del(5q-). All described patients with such a karyotypic abnormality belong to refractory anaemia subtype of MDS. The association between t(2;11) and del(5q-), which occurs frequently in MDS and specially in refractory anaemia, may not be an incidental event.

In fact, the break-points on the chromosomes 2, 5 and 11 allow the implication of the oncogenes N myc, C fms and of GM-CSF and IL_3 genes in the pathogenesis of the disease.

In fact, the GM-CSF and the IL_3 are growth stimulating factors of the proliferation and the differentiation of the granulocytic precursors. They also intervene in the recruitment process of the marrow progenitors[6,7]. In addition, the proliferation capacity of these progenitors is dependent on specific genes, including c-myc, c-myb and the c-fos oncogenes[8-10].

Cytogenetic studies and fluorescence in situ hybridation (FISH) technique have helped in understanding MDS pathogenesis, analysing regions of genome whose molecular biology is implicated in growth and proliferation of haematopoietic precursors[11].

The deleted part of the long arm of chromosome 5, having a variable length, has a great interest, particularly its zone within 5q14 and 5q35 region. However, most of the research teams who studied the deletions in the 5q- syndrome agree that the most common short deleted region is located in the 5q31 band[12-14].

The genes EGR1, IRF1 and a locus (D5S89) were incriminated in the affection, but their implication has not been proved yet. Conversely, a large number of genes controlling many growth factors and/or their receptors, including GM-CSF, IL5, and IL4 gene as well as the genes of PDGF, IL4, IL5, and M-CSF receptors and the oncogene C-fms were also subtracted.

The deletion of the long arm of the chromosome 5, particularly of 5q31 region, may be associated to the loss of some genes[18], because it has been proven that, in some cases, the missing sequence of the cytogenetically deleted chromosome was also missing in the homologous chromosome 5[19,20]. This may explain the cytomorphologic abnormalities and the cellular abortion due to apoptosis in MDS[21]. Deletions of chromosome 11 long arm are frequent, such as del (11q14) and del (11q23), while translocations involving chromosome 11 are extremely rare in MDS, as only 14 cases have been published[22]. The majority of cases with the t(2;11) translocation in MDS belong to refractory anaemia subtype and are associated to the loss of the long arm of the chromosome 5. The translocation t(2;11), as a sole cytogenetic event or in combination with 5q-, has been found in 12 cases of refractory anaemia and only once in acquired idiopathic sideroblastic anaemia and twice in AML which is not part of the MDS. These results suggest that t(2;11) is a characteristic abnormality of refractory anaemia with 5q-anomaly[23]. However, a study of the genome and eventually the product of this translocation is crucial to elucidate the role of this t(2;11) translocation in the pathogenesis of refractory anaemia.

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