## MLL intrachromosomal amplification in a pre-B acute lymphoblastic leukemia

**Haematologica 2007;** 88:(2)e28-e29

Recent reports have emphasized the role of MLL rearrangements in T and B lineage acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). Abnormalities of the MLL gene, located at 11q23, have been frequently described in acute leukemias (either as reciprocal translocations or as amplifications). Reciprocal translocations are the most common type, with over 30 different partner sites, reported in AML and ALL, the later mainly associated with childhood and a poor outcome[1]. Less frequently, whole genomic amplifications have been described as intrachromosomal amplifications or homogeneously staining regions (HSR) and extrachromosomal amplification or double minute chromosomes (dmin). The incidence of HSR and dmin in AML is extremely rare (1%), with only few reports of amplifications affecting MLL gene[2,3]. Regarding B-ALL, cases showing intrachromosomal amplifications (as HSR) have so far not been reported in adult patients. We communicate a case of pre-B ALL with an MLL amplification as an HSR.

A 86-year-old female was admitted to our hospital. On physical examination neither lymphadenopathies nor hepatosplenomegaly were detected. Laboratory findings revealed: Hb 91g/L, VCM 96fL, WBC count 2.2x10$^9$/L, with 37% of blasts and platelets 89x10$^9$/L. Seric immunofixation identified a monoclonal IgG kappa component and _2microglobulin 8.8 mg/L. The bone marrow aspirate showed 1% of plasma cells, granulopoiesis showed marked dysgranulopoietic features in >50% of it and an infiltration by 77% of medium-sized blast cells, with presence of nucleoli and an intense basophilic vacuolated cytoplasm. Blasts were negative for myeloperoxidase (MPO) and non-specific esterases. TDT, CD79a, CD19, CD20, CD34 and intracytoplasmic _ were positive and CD10, SIg and other B, T and myeloid markers including cytoplasmic MPO were negative. Ultrastructural examination of blasts showed negativity for MPO and for PPO. A diagnosis of pre-B ALL was established.

Bone marrow karyotype was: 44,XX,del(5)(q13q31), dic(6;17)(p25;q11), hsr(11)(pter_q23::hsr::q21::hsr::qter), -16,-17[18]/ 46,XX[2]. FISH studies with LSI MLL dual colour probe (Vysis, Downers Grove, IL) demonstrated multiple copies located in the hsr(11) (Figure 1). A MGG-FISH assay using the MLL probe showed that MLL amplification was confined to the blastic population, but was not present in other cells (Figure 2). The patient died shortly after being diagnosed.

MLL amplifications as HSR have never been described in adult ALL[4]. Two major series have communicated MLL amplifications in AML. Cuthbert *et al*[2] analyzed the presence of multiple copies of MLL in 12 acute leukemias; 11 were AML (five presented dmin and one case HSR) and one case was an ALL with multiple copies of MLL gene (by FISH). However, cytogenetic analysis and Southern blot studies failed to provide a confirmatory information. Michaux et al[3] reported 14 cases with myeloid malignancies, 8 patients with AML and six with MDS; one case presented dmin and two cases showed HSR. Regarding ALL, partial nontandem duplications have been described in the PER-377 cell line derived from an infant biphenotypic acute leukemia[5]. Nevertheless, larger amplifications of the entire MLL gene as dmin or HSR have never been reported in adult patients. The poor prognosis of this case is probably due, in part, to MLL amplification.

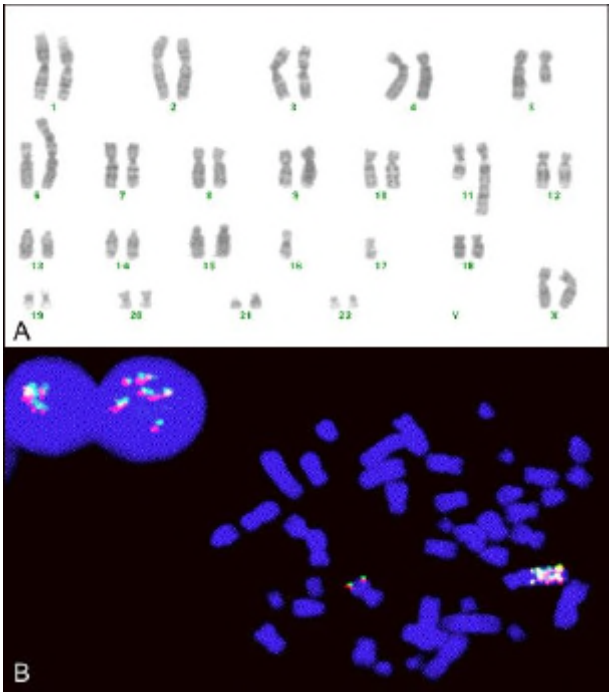


**Figure 1. A. Conventional karyotype of a patient affected with a pre-B acute lymphoblastic leukemia showing a complex karyotype. The presence of an hsr(11) is remarkable. B. Fluorescence in situ hybridization technique using a dual colour MLL probe. The presence of multiple copies of the MLL gene located in hsr(11) can be observed.**

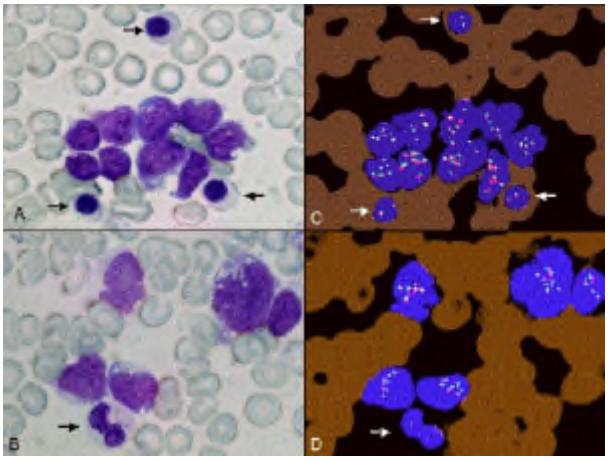


**Figure 2. A. Cytomorphology of May-Grünwald Giemsa stained blastic cells and three erythroblasts in the bone marrow. B. Cells were relocated after interphase FISH with dual color labelled MLL gene probe. Multiple hybridization signals can be observed in the blastic population while only two signals corresponding to the two normal #11 chromosomes can be seen in the three erythroblasts.**

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*Acknowledgments*

*This study was partially supported by the grant FIS 01/1424 from the spanish Ministerio de Sanidad y Consumo. The authors wish to thank Rosa Mª Vilà, Carme Melero and Mª José Maldonado for their excellent technical assistance.*

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