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A new translocation t(11;13)(q13;q14) in a mature B-cell neoplasm

We present the case of a man affected by an unclassified mature B-cell neoplasm with a bone marrow culture stimulated with TPA showing a 46,XY, t(11;13)(q13;q14)[14]/46,XY [6] karyotype. Fluorescent in situ hybridization demonstrated that the BCL1 oncogene is translocated (not rearranged) to chromosome band 13q14 and that a copy of D13S319 locus is deleted. To our knowledge, this is the first reported case with this novel cytogenetic aberration.

haematologica 2002; 87:777-778
(http://www.haematologica.ws/2002_07/777.htm)

The lymphomas and leukemias of B-lymphoid cells are heterogeneous diseases associated with different cytogenetic aberrations.¹ Translocations that involve genes controlling progression through the cell cycle have been described: cyclin D1 on chromosome 11q13 is involved in the t(11;14)(q13;q32) in mantle cell lymphoma (MCL),² and recently a new translocation t(6;14)(p21.1;q32.3) has been reported involving cyclin D3 in mature B-cell malignancies.³⁻⁵

Translocation t(11;14)(q13;q32) has been detected in MCL, multiple myeloma (MM) and chronic prolymphocytic leukemia (PLL). Cytogenetic abnormalities of chromosome band 13q14 reported in mature B-cell disorders include deletions and in some rare cases translocations, deletion 13q being one of the most frequent cytogenetic aberrations in B-cell chronic lymphocytic leukemia (B-CLL).⁶

Here we present a case with unclassified mature B-cell neoplasm showing a not previously reported translocation, t(11;13)(q13;q14), as a sole anomaly.⁷ The present case was studied by conventional cytogenetics and fluorescence in situ hybridization (FISH).

In November 1997, a 63-year old man was referred for study of a myelodysplasia. Physical examination revealed no abnormalities. Laboratory findings were: leukocyte count $3 \times 10^9/L$, Hb 13.1 g/dL, MCV 101 fL, and platelet count $104 \times 10^9/L$. A bone marrow aspirate showed a myelodysplastic syndrome (MDS), refractory cytopenia with trilineage dysplasia.

In October 2000 the patient had a white cell (WBC) count of $7.2 \times 10^9/L$ with 46% lymphocytes and in November 2001 the WBC was $12.2 \times 10^9/L$ with 69% of lymphocytes. Lymphocytes were small, with condensed chromatin, single nucleolus, without cytoplasmic prolongations and some presented plasmacytic differentiation (Figure 1). Immunological studies by flow cytometry showed the following: CD19⁺, CD5⁺, CD23⁺ weak (30%), FMC7⁺ weak, CD22⁺ weak, CD 79b⁺, CD10⁻, CD25⁺, CD11c⁺, CD38⁻, CD20⁺ bright, IgM⁺, IgD⁻, and monoclonal κ light chain with bright intensity (Matutes score 4/6).

In January 2002 the WBC count was $13.7 \times 10^9/L$ with 74% of lymphocytes. A bone marrow aspirate showed 40% lymphocytes, 18% red cells, 38% white cells and 4% plasma cells. Immunologic study of lymphocytes from peripheral blood revealed: CD5⁺ and CD23⁺ weak (24%) and an immunophenotypic profile in the majority of plasma cells (82%) suggested myeloma cells (CD38⁺, CD19⁺, and CD56⁺). The measurements of immunoglobulins in serum showed increased IgG and decreased levels of IgA and IgM: immunofixation revealed monoclonal heavy chain IgG and light chain κ . A 24-hour stimulated bone marrow culture with TPA showed a 46,XY, t(11;13)(q13;q14) [14]/46,XY [6] karyotype (Figure 2a). A diagnosis of an unclassified mature B-cell neoplasm was established. The patient did not receive any treatment.

FISH with locus-specific probes from LSI IgH/CCND1 or t(11;14)/BCL1/IgH (Vysis, Downers Grove, USA) 13q14 (D13S319) (Vysis) and 11q22.3-23.1 (ATM) (YAC clone 755b11) demonstrated that the BCL1 is translocated (not rearranged) into the derivative 13q (Figure 2b), ATM is translocated into 13q and the D13S319 locus is deleted (one copy).

To our knowledge this is the first reported case showing this cytogenetic aberration. It is noteworthy that in the present case two genes, both implicated in different B-cell malignancies, are involved, namely cyclin D1 and D13S319 locus; and that cyclin D1 is translocated and D13S319 locus is deleted. Deletion 13q is one of the most frequent aberrations observed in B-CLL, preferentially with typical morphology. It has been detected in MCL associated with t(11;14)(q13;q32), and is also found in MM related with a poor prognosis. It is interesting to remark that this patient could not be considered to have a B-CLL because the CD23 negativity and bright expression of CD20 and CD79b. In addition the diagnosis of MCL was discarded because BCL1/IgH rearrangement was not detected by FISH. Nevertheless, the finding of this novel cytogenetic aberration involving chromosomes 11 and 13 could explain the diagnosis of unclassified mature B-cell neoplasm according to the WHO classification.¹

More reports of patients with t(11;13)(q13;q14) are needed to determine the exact prognostic value of this new non-random chromosome anomaly and to study the exact role of these genes in the pathogenesis of lymphoid disorders.

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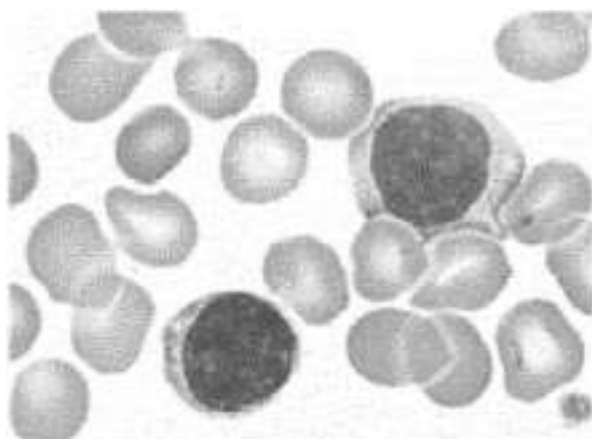


Figure 1. Peripheral blood smear, showing mature lymphocytes with condensed chromatin, single nucleoli and moderate cytoplasm with plasmacytic differentiation (MGG, magnification $\times 100$).

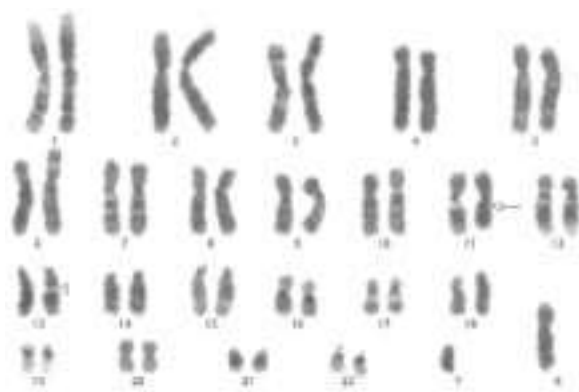


Figure 2a. Figure showing a 46,XY, t(11;13)(q13;q14) karyotype.

Funding: this study was partially supported by the grant FIS 01/1424 from the Spanish "Ministerio de Sanidad y Consumo".

Key words: translocation t(11;13), B-cell chronic lymphocytic leukemia, mantle cell lymphoma.

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Manuscript processing

This manuscript was peer-reviewed by two external referees and by Dr. Estella Matutes, who acted as an Associate Editor. The final decision to accept this paper for publication was taken jointly by Dr. Matutes and the Editors. Manuscript received March 6, 2002; accepted May 6, 2002.

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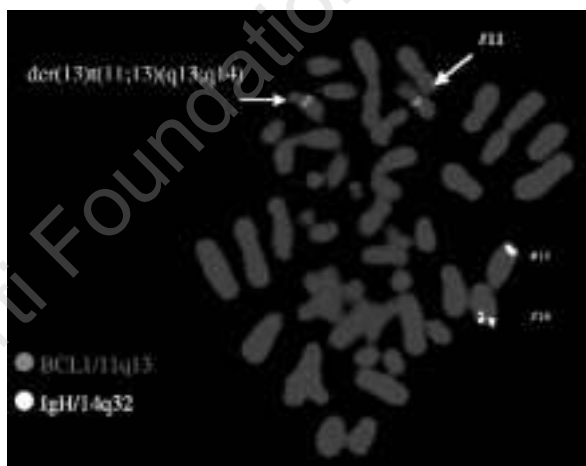


Figure 2b. FISH using dual color BCL1 (gray)/IgH (white) probe showing that IgH is not rearranged and BCL1 is translocated into 13q.