Interestingly, we did reveal an association between increased VEGF levels and thrombotic complications.

An increase in either intratumoral angiogenesis or serum levels of VEGF has been demonstrated in a variety of hematologic malignancies. The possible prognostic relevance of these measurements in chronic myeloproliferative disorders (CMD) has been reported by Musolino et al. who found significantly higher VEGF levels in CMD patients with vascular complications. It has also been reported that tumor-released VEGF activates endothelial cells to become prothrombotic causing platelet adhesion and activation. Other authors have observed endothelium activation in CMD patients and thromboembolic complications. Therefore, it is speculated that increased VEGF might be responsible for the endothelial activation. Other authors have reported increased VEGF in CMD accompanied by thrombocytosis that could limit the interpretation of this finding since platelets are a major source of VEGF.

We found increased VEGF levels in patients with PV without thrombocytosis and this increase was not correlated with the platelet count. Thus, in our study increased levels of VEGF might reflect a state of platelet activation and be responsible for occurrence of a thrombotic event. We, therefore, think that VEGF measurement might have a clinical use in categorizing high- and low-risk PV patients and be appreciated as an additional variable in clinical prognostic models. These data, if confirmed in larger studies, might also support the rationale for using angiogenesis inhibitors as antithrombotic agents.


References


10. Spivak JM, Colonna H, Scott H. Acute promyelocytic leukemia (APL) is characterized by the reciprocal translocation t(15;17(q22;q21), disrupting the PML and RAR-α genes, which are localized on chromosomes 15q22 and 17q21, respectively. The t(15;17) generates two chimeric genes: PML/RARα arises on der(15), whereas the reciprocal RARα/PML fusion is located on the der(17). Microdeletions on the derivative chromosome carrying the reciprocal fusion gene have been recently reported in some leukemia translocations such as t(9;22) in chronic myeloid leukemia (CML) and inv(16), as well as in t(8;21) and 11q23 abnormalities in acute myeloid leukemia (AML). In CML Ph+ and AML with inv(16) these microdeletions were associated with a worse prognosis. Microdeletions in APL cases have been recently investigated, by FISH, in 30 APL patients by Kolomietz et al., who utilized the Vysis LSI PML/RARα translocation probe. This study did not reveal microdeletions. The Vysis probe, however, is not able to detect deletions in der(17), as it was specifically designed to detect the expressed fusion gene on der(15) chromosome. Therefore, their conclusion on the absence of deletions on der(17) has no experimental support. In contrast, we used appropriate FISH probes, specifically designed to detect deletions in der(17). Thirty-four APL patients were enrolled at diagnosis. All cases were tested by conventional cytogenetic and RT-PCR analysis to assess the presence of the t(15;17) and of the fusion gene PML/RARα, respectively. Co-hybridization FISH experiments were performed by using a mixture of two probes (BAC RP11-247C2 and PAC RPS111Z21, from de Jong libraries), spanning the PML gene on chromosome 15 and RARα gene on chromosome 17, respectively (Figure 1a). Their precise positions were derived from the Ensembl database (http://wwwensembl.org). On metaphases of APL patients these probes generated two clear fusion signals on der(15) and on der(17) chromosomes in addition to single signals on normal 15 and 17 chromosomes (Figure 1b). The absence of a fusion signal on der(17) would reveal microdeletions on this chromosome. Twenty metaphases were evaluated for each patient. The analysis did not reveal any microdeletion, since an evident fusion signal on der(17) was observed in all analyzed metaphases.

In our series there was 1(3%) case with cryptic PML/RARα fusion gene created by an insertional event, which is in agreement with the frequency of this abnormality in APL cases reported in the literature. In fact, this patient was apparently normal chromosomes 15 and 17 by conventional cytogenetic analysis while RT-PCR revealed expression of PML/RARα. Fluorescent in situ hybridization (FISH) experiments showed an abnormal hybridiza...

Manuscript processing

This manuscript was peer-reviewed by two external referees and by Dr. Jerry L. Spivak, who acted as an Associate Editor. The final decision to accept this paper for publication was taken jointly by Dr. Spivak and the Editors. Manuscript received March 1, 2002; accepted May 6, 2002.

haematologica vol. 87(7):july 2002
tion pattern: PAC RP5-1112G21 gave the classical splitting [signals on both der(17) and der(15); Figure 1c], while BAC RP11-247C2 showed signals of equal intensity on normal chromosome 15 and on der(15). No RP11-247C2 signal was detected on der(17). Co-hybridization of chromosome 15 WCP with RP5-1112G21 revealed a cryptic insertion of RAR\(\alpha\) gene in one chromosome 15.

The present study suggests that t(15;17) is not accompanied by any deletion in der(17). Very small deletions (a few kb), escaping FISH detection cannot be excluded. Our conclusion could also be biased by the relatively small number of patients analyzed, and confirmation on larger studies are needed. Statistical analysis, however, allows exclusion of the deletion in more than 9% of patients with a 95% confidence level.10

References


Figure 1. (a) The figure shows the position of probes RP11-247C2 and RP5-1112G21 in respect to PML and RAR\(\alpha\) genes. The size of both probes is approximately 150 Kb. (b) FISH pattern in a metaphase characterized by a t(15;17) rearrangement without detectable deletion. (c) FISH experiment performed using the same probes in the case showing a PML/RAR\(\alpha\) insertion. BAC RP11-247C2 showed signals of equal intensity on normal chromosome 15 and on der(15), while PAC RP5-1112G21 gave signals on both der(17) and der(15).
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. 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 as follows: WBC count was 13.1 g/dL; MCV 101 fL; and platelet count 104 × 10^9/L. A bone marrow aspirate showed a myelodysplastic syndrome (MDS), refractory cytopenia with multilineage dysplasia.

In October 2000 the patient had a white cell (WBC) count of 7.2 × 10^9/L with 46% lymphocytes and in November 2001 the WBC was 12.2 × 10^9/L with 69% of lymphocytes. Lymphocytes were small, with condensed chromatin, single nucleoli, without cytoplasmic prolongations and some presented plasmacytoid differentiation (Figure 1). Immunological studies by flow cytometry showed the following: CD19+, CD5+, CD23+ weak (30%), FM C7+ 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 × 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 (CD38+, CD19+, CD20+, IgM+ light chain).

The lymphomas and leukemias of B-lymphoid cells are heterogeneous diseases associated with different cytogenetic aberrations: two 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)1, and recently a new translocation t(6;14) (p21.1;q32.3) has been reported involving cyclin D3 in mature B-cell malignancies.2-5

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)/46,XY [6] karyotype. Fluorescent in situ hybridization demonstrated that the BCL1 oncogene is translocated (not rearranged) into the derivative 13q (Figure 2b), ATM is translocated into 13q and the derivative 13q (Figure 2b). The probe for 13q showed increased IgG and decreased levels of IgA and IgM; immunohistochemistry 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)/46,XY [6] karyotype (Figure 2b). A diagnosis of an unclassified mature B-cell neoplasm was established. The patient did not receive any treatment.

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

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. 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 as follows: WBC count was 13.1 g/dL; MCV 101 fL; and platelet count 104 × 10^9/L. A bone marrow aspirate showed a myelodysplastic syndrome (MDS), refractory cytopenia with multilineage dysplasia.

In October 2000 the patient had a white cell (WBC) count of 7.2 × 10^9/L with 46% lymphocytes and in November 2001 the WBC was 12.2 × 10^9/L with 69% of lymphocytes. Lymphocytes were small, with condensed chromatin, single nucleoli, without cytoplasmic prolongations and some presented plasmacytoid differentiation (Figure 1). Immunological studies by flow cytometry showed the following: CD19+, CD5+, CD23+ weak (30%), FM C7+ 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 × 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 (CD38+, CD19+, CD20+, IgM+ light chain).

The lymphomas and leukemias of B-lymphoid cells are heterogeneous diseases associated with different cytogenetic aberrations: two 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)1, and recently a new translocation t(6;14) (p21.1;q32.3) has been reported involving cyclin D3 in mature B-cell malignancies.2-5

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)/46,XY [6] karyotype. Fluorescent in situ hybridization demonstrated that the BCL1 oncogene is translocated (not rearranged) into the derivative 13q (Figure 2b), ATM is translocated into 13q and the derivative 13q (Figure 2b). A diagnosis of an unclassified mature B-cell neoplasm was established. The patient did not receive any treatment.

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

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. 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 as follows: WBC count was 13.1 g/dL; MCV 101 fL; and platelet count 104 × 10^9/L. A bone marrow aspirate showed a myelodysplastic syndrome (MDS), refractory cytopenia with multilineage dysplasia.

In October 2000 the patient had a white cell (WBC) count of 7.2 × 10^9/L with 46% lymphocytes and in November 2001 the WBC was 12.2 × 10^9/L with 69% of lymphocytes. Lymphocytes were small, with condensed chromatin, single nucleoli, without cytoplasmic prolongations and some presented plasmacytoid differentiation (Figure 1). Immunological studies by flow cytometry showed the following: CD19+, CD5+, CD23+ weak (30%), FM C7+ 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 × 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 (CD38+, CD19+, CD20+, IgM+ light chain).

The lymphomas and leukemias of B-lymphoid cells are heterogeneous diseases associated with different cytogenetic aberrations: two 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)1, and recently a new translocation t(6;14) (p21.1;q32.3) has been reported involving cyclin D3 in mature B-cell malignancies.2-5

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)/46,XY [6] karyotype. Fluorescent in situ hybridization demonstrated that the BCL1 oncogene is translocated (not rearranged) into the derivative 13q (Figure 2b), ATM is translocated into 13q and the D13S319 locus is deleted. To our knowledge, this is the first reported case with this novel cytogenetic aberration.