leukemias with myelodysplasia seem to be indistinct. Whether or not this novel gene is rearranged with the TEL gene in this translocation requires further elucidation. The limits between MDS and myeloproliferative syndromes as well as truly acute non-lymphoblastic leukemias with myelodysplasia seem to be indistinct and new entities could be defined provided that non-random chromosomal abnormalities can be demonstrated in these patients.

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Cytogenetic and molecular studies of variant Ph' translocations

We describe the cytogenetic and molecular studies of three simple variant Ph'-translocations: t(11;22) (p15;q11), t(13;22)(p11;q11) and t(20;22) (q12;q11), representing only 1% of our chronic myeloid leukemia cases. Breakpoints 13p11 and 20q12 have not previously been reported. All cases showed bcr/abl rearrangement, indicating the participation of chromosome 9 in spite of the normal cytogenetic appearance.

Sir,

The Ph' chromosome is present in hematopoietic cells from about 95% of patients with chronic myeloid leukemia (CML). Variant forms of the t(9;22) have been found in a low percentage of cases (5-10%). Two variant forms have been recognized: simple (the segment lost from 22q is translocated into a chromosome other than 9) and complex (three or more chromosomes are involved).1 In spite of the normal cytogenetic appearance of chromosome 9 in simple variants, some papers reported detection of the bcr/abl rearrangement by polymerase chain reaction (PCR) or in situ hybridization techniques.2

We present the cytogenetic and molecular studies of three patients with simple variant translocations, two of whom with points not previously described. These findings are uncommon events in our population, representing only 1% (3/300) of all cytogenetically analyzed CML patients.

The three patients had a diagnosis of CML and two of them were in accelerated phase treated with hydroxyurea. One patient in chronic phase received high dose interferon (5MU/m2/d) and achieved a hematologic complete response. None of them reached cytogenetic remission. After a period of 2 to 5 years all of them evolved to blast crisis and died after the failure of AML treatment.

The cytogenetic analysis was performed on bone marrow cultures of 24-48 hrs without mitogen and the karyotype was analyzed by G-banding.3 For molecular study total RNA was extracted from peripheral blood and processed by RT (reverse transcriptase)-PCR.4 Cytogenetic, molecular and clinical studies are summarized in Table 1.

The chromosome bands involved in our simple variant Ph' translocations were: 11p15, 13p11 and 20q12 (Figure 1a). The band 11p15 has been reported on several occasions indicating a frequent site in both types of variant forms in CML. Bands 13p11 and 20q12, to our knowledge, have not been documented in variant Ph' translocations, although nearby bands such as 13p13 and 20q13 have been reported.

The three translocations showed the involvement of chromosome 22 and a chromosome other than 9. Molecular analysis detected the bcr/abl rearrangement in the three cases (Figure 1b).

The literature contains controversies about the significance of the Ph' variant translocations in the clinical course. Potter et al. found a shorter chronic
phase in patients with Ph' variant translocations, while other authors showed that survival was not affected. Our patients had the expected survival rate without remarkable differences with respect to the classical Ph' positive evolution.

The molecular data indicate that most Ph' variant translocations involve three or more chromosomes and always both 22q11 and 9q34, resulting in a bcr/abl junction.2,3,10 These findings are probably the reason for the unchanged prognosis and clinical follow-up compared with common cases.

In our three cases, molecular analysis demonstrated the bcr/abl rearrangement. We detected a b2a2 junction in the case with t(11;22) and b3a2 in the other two cases. These results indicate the involvement of chromosomes 9 and 22 in addition to other chromosomes. Our findings together with literature reports indicate that the simple variant translocations could be reclassified as complex ones.

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Key words
Variant Ph' translocations, bcr/abl fusion gene, chronic myeloid leukemia.

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Complete molecular remission induced by rituximab in a patient with diffuse large cell lymphoma

Along with the comprehensive data concerning our institutional experience on the use of rituximab for treatment of non-Hodgkin’s lymphoma, we describe the first case of molecular remission induced by the chimeric anti-CD20 monoclonal antibody in a diffuse large cell lymphoma patient.

Sir,

The treatment recommendations for low-grade non-Hodgkin’s lymphomas (LG-NHL) remain controversial today. 

The success of these patients has not changed in more than 20 years. Rituximab is a chimeric anti-CD20 monoclonal antibody containing human IgG1 and κ constant regions with murine variable regions. The CD20 antigen is expressed consistently on nearly all human B-cells and most B-cell lymphomas present this antigen on the cell surface. Rituximab induces responses in around half of the patients with follicular LG-NHL and has also demonstrated activity in intermediate-grade and high-grade NHL.

We report here our institution’s experience, in terms of clinical results, on the treatment of 12 patients with relapsed B-cell lymphoma. The patients, 8 males and 4 females, ranged from 35 to 68 years of age (median age: 50 years). Four patients had B symptoms. The distribution of the histologic subtypes was as follows: follicular lymphoma, 7 patients; small lymphocytic lymphoma, 3 patients; mantle cell lymphoma, 1 patient; and diffuse large cell lymphoma, 1 patient. Four patients had stage III disease according to the Ann Arbor staging system and 8 patients were in stage IV with bone marrow involvement. No patient had bulky disease. The patients had received a median of 3 prior, heterogeneous regimens (range 2-5). The median time from diagnosis was 3.5 years. All patients received 4-hour infusions of rituximab (375 mg/m²) once weekly for four doses over a period of 22 days.

Clonal IgH rearrangements were amplified by polymerase chain reaction starting from genomic DNA and using VH.L consensus primers and a JH.D primer as described elsewhere. The sensitivity of detection of tumor cells ranged from $10^{-3}$ to $10^{-5}$. Of the 12 patients, 4 (34%) achieved a complete response (CR) and 3 (25%) a partial response (PR) with an overall response rate (CR plus PR) of 59% (7/12). The median time to response was 45 days with continued improvement in response at 2 months. Of the stage IV patients with bone marrow involvement, 4/8 (50%) obtained a response (3 CR and 1 PR). Of the 7 follicular lymphoma patients, 3 (43%) achieved a CR and 2 (28.5%) a PR with a global response of 71.5%.

The patient with diffuse large-cell lymphoma achieved a molecular CR in addition to CR. He was given second-line treatment with an autologous bone marrow transplantation obtaining a good clinical PR with the persistence of molecular disease. Two months after rituximab treatment he showed a clinical CR and after 3 months molecular disease was no longer present in either peripheral blood or bone marrow (see Figure 1). At present, after 12 months this patient is still alive in CR. It is noteworthy that in this case the first CR had lasted only 4 months. This particular aspect is very interesting because it is the first evidence of a molecular disease negativity being obtained in diffuse large cell lymphoma by rituximab.

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Key words

Rituximab, aggressive lymphoma, molecular remission

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