

received different protocols of induction chemotherapy including an anthracycline (daunorubicin or idarubicin) alone or in combination with cytosine arabinoside (Some biological and clinical data are given in Table 1). The 9 patients (#1-9) achieved CR after different schedules of ablative induction and consolidation chemotherapy protocols (Table 1). All 9 patients who achieved clinical remission are currently alive in first (7 cases) (77%) or second (2 cases) (23%) CR (Figure 1), confirming that AML with inv(16) is curable by ablative therapy in a high percentage of cases. Two patients experienced relapse (#5 and 9 in Table 1) but they achieved a second CR, one of these lasting more than 36 months. On these nine patients, remission bone marrow aspirates were obtained after achievement of CR and used for molecular analysis.⁴ Cytogenetic studies and RT-PCR analysis were performed as reported.⁴ Experiments using inv(16) RNA in serial dilution of total RNA from normal individual were also conducted: the level of sensitivity of type A fusion sequence amplification after nested PCR was of 1 tumor cell in 10⁵-10⁶ non-neoplastic cells.⁴ At diagnosis, chimeric cDNAs were detected after amplification in all 9 patients (Table 1). Only one type out of nine reported chimeric transcripts was found, representing 1921 position fusion point within MYH11 spliced to position 495 of CBF β (type A). This finding is in line with the concept that AML with inv(16) is strictly associated with the type A transcript.^{3,4} The results of RT-PCR analysis in remission samples are schematically represented in Figure 1. In no cases, were CBF β /MYH11 transcripts visible on the ethidium bromide gels. In the 2 cases who experienced relapse, (patients #9 and #13), no prediction of re-emerging MRD was possible, due to the fact that PCR (negative) was last performed 8 and 12 months, respectively before relapse.

Recent studies indicate that molecular monitoring of the CBF β /MYH11 fusion transcript in AML could allow identification of patients who need further antileukemic therapy.⁵⁻¹⁰ On the other hand, we⁴ and others⁵ have reported that AML with inv(16)⁺ may be associated with eradication of cells carrying the specific CBF β /MYH11 rearrangement, indicating that: 1) PCR negativity should be considered the therapeutic goal in these patients; 2) the cure of AML inv(16)⁺ by chemotherapy is accompanied by elimination, at least below our RT-PCR sensitivity levels, of residual cells expressing the CBF β /MYH11 transcript. Quantitative PCR analysis could be useful for improving the significance of MRD.⁹ This means that the RT-PCR assay is a useful prognostic tool not only in the induction and consolidation treatment phases, but also during long-lasting follow-up.¹⁰

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Funding

This study was supported by the Associazione Italiana per la Ricerca sul Cancro (A.I.R.C.), by the Italian C.N.R. target project #98.00526.CT04, by a "A.I.L. 30 Ore per la Vita" target project and by a M.U.R.S.T. 40% grant.

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Myelofibrosis in myeloid malignancies with 3q26 cytogenetic abnormalities

3q abnormalities define a subtype of myeloid malignancies characterized by similar clinical, morphologic and cytogenetic features, poor response to therapy and short survival. Trilineage myelodysplasia, affecting particularly the megakaryocytic line, is

usually present. We describe five patients with myeloid malignancies and 3q26 abnormalities in whom bone marrow biopsy showed reticulin fibrosis, a feature rarely reported.

Sir,

We read with interest the recent paper published by Testoni *et al.*¹ on the clinical and biological features of patients with acute myeloid leukemias (AML) with 3q21 and 3q26 abnormalities. Our group recently published similar results in a series of 10 patients with 3q26 rearrangements.² However, in 5 of our patients (4 of them included in the series referred to above and 1 recently diagnosed) marked reticulin fibrosis was observed in the bone marrow biopsy, a feature that, to our knowledge, has been scarcely referred in these patients.

Between January 1990 and July 1999, 340 patients were diagnosed with myeloid malignancies (*de novo* and secondary acute non-lymphoblastic leukemias, myelodysplastic and myeloproliferative syndromes) in our center; 12 of them showed a 3q alteration involving band 3q26. Their median age was 63 years (range 36-79) and 6 of the patients were male. The main clinical and analytic parameters of the first 10 cases have been described elsewhere.² Bone marrow biopsy was performed in 5 out of the 12 patients because of a dry tap, and in all of them marked (grade III) reticulin fibrosis was observed. In addition, collagen fibrosis was observed in one case. Two of them were diagnosed as having *de novo* AML (M0 and M1 FAB subtypes) and two had a secondary leukemia (one secondary to essential thrombocythemia and one to refractory anemia). The remaining patient had a refractory anemia with excess of blasts (RAEB). The platelet count was $>100 \times 10^9/L$ only in the patient diagnosed with RAEB. The cytogenetic study using a rapid band technique³ revealed *inv*(3)(q21;q26) in 2 cases, *t*(2;3)(p21;q26) in one, *t*(3;12)(q26;p12) in one and *t*(3;3)(q21;q26) in the remaining. In addition to the 3q alteration, monosomy of chromosome 7 (3 patients), 5q- (2 patients) and trisomy 8 (1 patient) were present. All five patients had an increase in the number of megakaryocytes: 4 presented with small sized megakaryocytes with hypolobulated nuclei and one with large megakaryocytes with multilobulated nuclei. Three patients received intensive chemotherapy (idarubicin and cytarabine) and complete remission was achieved in two of them, but one died due to leukemia relapse. Only one patient is alive, currently receiving consolidation chemotherapy.

3q abnormalities define a subtype of myeloid malignancies characterized by similar clinical, morphologic and cytogenetic features, poor response to therapy and short survival.^{1-2,4-5} Trilineage myelodysplasia, particularly predominant in the megakaryocytic line, is usually present,^{1,2,4-6} giving rise to clusters of small megakaryocytes. This increase in the number of megakaryocytes could explain the increased platelet count described in some patients.^{1,5,7,8} The presence of reticulin fibrosis, observed in the five patients of our series of 3q26 rearrangements in whom a bone marrow biopsy was performed should be pointed out. In a search performed of the MEDLINE® database (from 1982 to September 1999, key words *3q* and *fibrosis*) we have found

this morphologic feature reported in 9 out of 14 cases with acute non-lymphocytic leukemia and 3q abnormalities (in 5 of them the 3q26 band was involved).⁸ This feature was also seen in a patient with chronic myelomonocytic leukemia and in another with primary myelofibrosis:^{9,10} the first case showed a *t*(3;6), but the involved band was q12;⁹ and in the second patient the *t*(2;3)(p21;q26) was present.¹⁰ Our findings suggest that bone marrow biopsy should be performed in patients with myeloid malignancies with 3q26 abnormalities to determine whether reticulin fibrosis could be an additional feature in these patients.

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Key words

3q alterations, reticulin fibrosis, myeloid malignancies.

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