Clinical and cytogenetic findings in 10 patients with deletions of the long arm of chromosome 5 (5q-) are reported. Five cases had refractory anemia, the preleukemic syndrome, or refractory anemia with an excess of blasts; in all but one, the 5q- was the single initial abnormality. Three patients had overt leukemia; in all, the 5q- was accompanied by additional anomalies. Two patients had a myeloproliferative disorder. In one of these, a case of polycythemia vera, the 5q- appeared secondarily to other karyotypic abnormalities and concomitantly with transformation into a "spent phase." The deletions were interstitial in most cases, and even if the size of the deletion varied, the region q15-q31 was lost in all cases except 2.

Bone marrow from all cases except one showed a marked increase in the number of megakaryocytes. A survey of the literature yielded a total of 69 evaluable patients with 5q- deletions, including the present series. The 5q- has now been observed in a wide spectrum of hematologic disorders. However, most cases had either preleukemia (39%) or leukemia (46%). When detected during preleukemia, the 5q- usually appeared alone (74%), while during overt leukemia it regularly was accompanied by other abnormalities (88%).

 Besides the Ph1 chromosome in chronic granulocytic leukemia, a close relationship between a chromosomal abnormality and a specific hematologic disease has been established in only a few instances, e.g., t(8;21) in acute nonlymphocytic leukemia1 and t(15;17) in acute promyelocytic leukemia.2 Other abnormalities, e.g., trisomy 8, partial trisomy for the long arm of chromosome 1, and the 20q- deletion, have been associated unspecifically with a broader spectrum of disorders.3-6 A few years ago, the clinical and cytogenetic characteristics of a "5q- syndrome" were reported7,8 as a further example of a close association between a chromosome abnormality and a distinct clinical entity.

The aim of this article is to report the clinical and cytogenetic findings in 10 patients with 5q- deletions and to review the relevant literature in an attempt to evaluate the significance of the 5q- as a marker of a specific clinical syndrome.

Materials and Methods

The patients included in this report were derived from a population of cytogenetically examined cases presenting mainly with myeloproliferative disorders and preleukemic conditions.

As a rule bone marrow chromosomes were examined in direct preparations with conventional techniques. When evaluable metaphases could not be obtained by this method, marrow was also studied after 48-hr incubation (see Table 3). Q- and G-banding techniques were performed according to slightly modified current techniques.6,9 Peripheral blood chromosomes were examined in phytohemagglutinin-stimulated leukocyte cultures after a 48-hr incubation. Chromosome identification and karyotypic nomenclature were in accordance with the recommendations of the Paris Conference.10

Measurements of bone marrow cellularity, megakaryocyte number, and mean megakaryocyte area were made on paraffin-embedded sections of aspirated sternal marrow, as previously described.12

Results

Clinical and Morphological Findings

The clinical course of the 10 patients in the present series (4 women and 6 men, age 47-69 yr) is briefly summarized in Table 1.

In 5 patients the diagnosis at the time of the first cytogenetic examination were refractory anemia (case 2), the preleukemic syndrome as defined by Linman and Bagby13 (cases 1, 4 and 6), or refractory anemia with excess of blasts (RAEB) as defined by Bennett et al.14 (case 7). In cases 4 and 7, acute nonlymphocytic leukemia was diagnosed 9 and 12 mo later, respectively. Case 4 was a chemist and had had a long exposure to organic solvents.

Three other patients (cases 5, 8, and 9) were examined during overt leukemia only. In case 5 the leukemia was preceded by a hypoplastic anemia of 4 yr duration. Case 8 was treated for more than 4 yr for multiple myeloma with a small daily dose of melphalan. The last year before the diagnosis of leukemia, he passed through a preleukemia-like phase characterized by hypercellular bone marrow, sideroblastic anemia, and a gradually more marked granulocytopenia and thrombocytopenia.

Two patients had a myeloproliferative disorder. In case 3 this was characterized by a marked thrombocytosis and refractory anemia, and melphalan had been administered intermittently for 5 yr to control the...
Table 1. Diagnosis and Clinical Course of 10 Patients With 5q− Deletions

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age/Sex</th>
<th>Time of Diagnosis</th>
<th>Clinical Course</th>
<th>Time of Death</th>
<th>Cause of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>60/M</td>
<td>7/77</td>
<td>1977–80 preleukemic syndrome</td>
<td>Alive</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>61/F</td>
<td>1/73</td>
<td>1973–80 refractory anemia</td>
<td>Alive</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>62/F</td>
<td>1/74</td>
<td>1974–80 myeloproliferative syndrome (thrombocytosis, refractory anemia); melphalan since 1975</td>
<td>Alive</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>51/M</td>
<td>6/73</td>
<td>1973–76 preleukemic syndrome; 6/76 AML (M2)</td>
<td>2/77</td>
<td>Leukemia</td>
</tr>
<tr>
<td>5</td>
<td>59/M</td>
<td>5/76</td>
<td>1976–80 hypoplastic anemia; 6/80 AML (M2)</td>
<td>8/80</td>
<td>Leukemia</td>
</tr>
<tr>
<td>6</td>
<td>61/F</td>
<td>9/77</td>
<td>1977–79 preleukemic syndrome</td>
<td>12/79</td>
<td>Cerebral hemorrhage</td>
</tr>
<tr>
<td>7</td>
<td>69/F</td>
<td>8/76</td>
<td>1976–77 refractory anemia with excess of blasts; 11/77 AML (M2; diagnosed at autopsy)</td>
<td>11/77</td>
<td>Leukemia</td>
</tr>
<tr>
<td>8</td>
<td>47/M</td>
<td>6/68</td>
<td>1968–75 myelomatosis, treated with melphalan; 12/75 AML (M6)</td>
<td>1/76</td>
<td>Leukemia</td>
</tr>
<tr>
<td>9</td>
<td>60/M</td>
<td>1/75</td>
<td>1970–75 polycythemia vera treated with phlebotomies alone; 2/76 development of &quot;spent phase&quot; (anemia, granulocytic hyperplasia, focal myelofibrosis, myeloid metaplasia)</td>
<td>7/75</td>
<td>Leukemia</td>
</tr>
<tr>
<td>10</td>
<td>60/F</td>
<td>9/70</td>
<td>1970–76 polycythemia vera treated with phlebotomies alone; 2/76 development of &quot;spent phase&quot;</td>
<td>5/76</td>
<td>Progressive disease</td>
</tr>
</tbody>
</table>

AML, acute myeloid leukemia, classified according to the FAB criteria.14

Platelet level and diminish the need for transfusions. Case 10 had polycythemia vera, which, after 6 yr of therapy with phlebotomies alone, transformed into a "spent phase" with an accelerated terminal course.

The peripheral blood and bone marrow findings at the time the 5q− deletion was first demonstrated are presented in Table 2. All patients had a moderate to marked anemia. The initial WBC count was below the normal range in four-fifths of the preleukemic and two-thirds of the leukemic cases. A moderate elevation of the platelet level was found in 2 patients (cases 1 and 6), while the thrombocytosis in case 3 exceeded $1.000 \times 10^9$/liter. In case 4, the platelet level remained normal despite fully developed leukemia.

Histologic examination of the bone marrow revealed an increase in the number of megakaryocytes in all cases except case 7. The megakaryocytic hyperplasia was the dominant feature of the marrow in case 3 and was prominent in some of the preleukemic patients (cases 2 and 4) and, more remarkable, also in all the leukemic patients (cases 4, 5, 8, 9). The size of the megakaryocytes was smaller than normal in all

Table 2. Hematologic Findings in Peripheral Blood and Bone Marrow From 10 Patients With 5q− Deletions at the Time When the Chromosome Abnormality Was First Observed

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Hemoglobin (g/liter)</th>
<th>White Blood Cells (x 10^9/liter)</th>
<th>Platelets (x 10^9/liter)</th>
<th>Erythropoiesis (%)</th>
<th>Myeloblasts + Promyelocytes (%)</th>
<th>Cellularity (%)</th>
<th>No. of Megakaryocytes (/sq mm)</th>
<th>Mean Megakaryocyte Area (sq μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>104</td>
<td>2.9</td>
<td>540</td>
<td>19</td>
<td>9</td>
<td>50</td>
<td>47</td>
<td>270</td>
</tr>
<tr>
<td>2</td>
<td>96</td>
<td>3.3</td>
<td>232</td>
<td>15</td>
<td>10</td>
<td>70</td>
<td>143</td>
<td>162</td>
</tr>
<tr>
<td>3</td>
<td>80</td>
<td>10.5</td>
<td>1.300</td>
<td>2</td>
<td>7</td>
<td>95</td>
<td>210</td>
<td>221</td>
</tr>
<tr>
<td>4a</td>
<td>70</td>
<td>2.5</td>
<td>100</td>
<td>3</td>
<td>1</td>
<td>40</td>
<td>84</td>
<td>158</td>
</tr>
<tr>
<td>5</td>
<td>49</td>
<td>3.7</td>
<td>48</td>
<td>0</td>
<td>33</td>
<td>60</td>
<td>84</td>
<td>152</td>
</tr>
<tr>
<td>6</td>
<td>73</td>
<td>1.9</td>
<td>530</td>
<td>25</td>
<td>4</td>
<td>65</td>
<td>54</td>
<td>225</td>
</tr>
<tr>
<td>7</td>
<td>129</td>
<td>12.5</td>
<td>180</td>
<td>14</td>
<td>10</td>
<td>95</td>
<td>15</td>
<td>221</td>
</tr>
<tr>
<td>8</td>
<td>82</td>
<td>3.7</td>
<td>19</td>
<td>53</td>
<td>3</td>
<td>100</td>
<td>132</td>
<td>236</td>
</tr>
</tbody>
</table>

(Leukemic erythroblasts)

| 9           | 65                   | 5.5                              | 20                       | 15 + 20% monocyto... |
| 10          | 108                  | 23.6                             | 60                       | 15                | 6                             | 100            | 57                          | NE                             |

Control subjects (n = 25)11

*At the time when leukemia was diagnosed.

NE, not examined.
cases examined (Table 2). Many cells had only 1–2 nuclear lobes. In 2 patients (cases 3 and 8), ultrastructural examination of the megakaryocytes showed an abnormal accumulation of demarcation membranes and defects in the formation of membrane complexes.

**Cytogenetic Findings**

The peripheral blood lymphocytes showed a normal karyotype in all patients. The results from the bone marrow chromosome studies are summarized in Table 3, and the appearance of chromosomes 4 and 5 from each patient are shown in Fig. 1. In cases 1–7 the deleted part of the long arm of chromosome 5 was of roughly the same size. The abnormality was interpreted as an interstitial deletion in 4 patients, with the proximal break in q13 (cases 1, 2, 4) or q15 (case 6), and the distal break in q31 (cases 1, 6), q33 (case 4), or q34 (case 2). In three patients (cases 3, 5, 7), a terminal deletion (break in q15) was considered most probable, but it cannot be ruled out that these deletions were also interstitial with a small terminal fragment remaining (q15q34–35?). Case 8 had lost almost the whole long arm (break in region q11). Thus, a loss of the central portion of the long arm, i.e., region 5q15–5q31 was common to all 8 patients. Two cases differed from this pattern and had a distal and terminal deletion with a break in the region q31 (cases 9 and 10).

In cases 1–4, the initial abnormal finding was a clone with 5q− as the single anomaly. Subsequently, other clonal abnormalities occurred in all these cases. In case 4, a second study after the patient had developed acute leukemia showed persistence and increase (from 32% to 86%) of the 5q− clone and addition of a small clone (10%) with −5. In cases 1–3, repeated examinations over several years have revealed the emergence and persistence of further abnormal clones in addition to the 5q− clone. All 3 patients developed trisomy 8; case 2 also developed cells with a 46,XX,t(9;11) karyotype (Table 3). In none of the

<table>
<thead>
<tr>
<th>Patient</th>
<th>Date of Study (mo/yr)</th>
<th>Method</th>
<th>No. of Cells Karyotyped</th>
<th>Normal Cells (%)</th>
<th>Cells in Abnormal Cell Line(s) (%)</th>
<th>Karyotype of Abnormal Cell Line(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9/77</td>
<td>Dr</td>
<td>32</td>
<td>28</td>
<td>72</td>
<td>46, XY, del (5) (q13q31)</td>
</tr>
<tr>
<td>2</td>
<td>10/73</td>
<td>Cult</td>
<td>26</td>
<td>4</td>
<td>96</td>
<td>46, XX, del (5) (q13q34)</td>
</tr>
<tr>
<td>3</td>
<td>9/75</td>
<td>Dr</td>
<td>23</td>
<td>43</td>
<td>57</td>
<td>46, XX, del (5) (q13q31)</td>
</tr>
<tr>
<td>4</td>
<td>9/75</td>
<td>Cult</td>
<td>23</td>
<td>68</td>
<td>32</td>
<td>46, XY, del (5) (q13q33)</td>
</tr>
<tr>
<td>5</td>
<td>6/70</td>
<td>Cult</td>
<td>14</td>
<td>0</td>
<td>100</td>
<td>47, XY, del (5) (q157), +21</td>
</tr>
<tr>
<td>6</td>
<td>10/78</td>
<td>Cult</td>
<td>27</td>
<td>56</td>
<td>44</td>
<td>46, XX, del (5) (q15q31), del (11) (q147)</td>
</tr>
<tr>
<td>7</td>
<td>11/76</td>
<td>Cult</td>
<td>25</td>
<td>0</td>
<td>8/92</td>
<td>46, XX, del (5) (q15q31)/49–51, XX, +1, del (5) (q157), +11, +14, +22, +mar</td>
</tr>
<tr>
<td>8</td>
<td>1/76</td>
<td>Dr</td>
<td>25</td>
<td>4</td>
<td>72/24</td>
<td>45, XY, del (5) (q11), −7/45, XY, del (5) (q11), −7, ins (3;3) (q21q27; q12)</td>
</tr>
<tr>
<td>9</td>
<td>2/75</td>
<td>Cult</td>
<td>33</td>
<td>0</td>
<td>70</td>
<td>43–46, X, −Y, del (5) (q31), −7, +18, −20 (plus additional variable changes)</td>
</tr>
<tr>
<td>10</td>
<td>6/72*</td>
<td>Dr</td>
<td>17</td>
<td>0</td>
<td>100</td>
<td>47, XY, +mar, F7−</td>
</tr>
<tr>
<td>11</td>
<td>5/75</td>
<td>Dr</td>
<td>38</td>
<td>0</td>
<td>76/18/8</td>
<td>47, XY, +del (1) (p21), del (20) (q11)/46, XY, del (20) (q11)/47, XY, +9, del (20) (q11)</td>
</tr>
<tr>
<td>3/76</td>
<td>Dr</td>
<td>38</td>
<td>0</td>
<td>63/11/26</td>
<td>47, XY, +del (1) (p21), del (20) (q11)/47, XY, +9, del (20) (q11)/47, XY, +del (1) (p21), del (5) (q31), del (20) (q11)</td>
<td></td>
</tr>
</tbody>
</table>

*No banding studies were performed.

Dr, direct preparations; Cult, after 48-hr incubation.
latter 3 cases was the development of new clonal abnormalities associated with any obvious change in the clinical course.

In cases 5–9, more complex chromosome abnormalities were present as early as the initial bone marrow study. In case 7, a small (8%) 46,XX,5q– clone was observed, but most cells had a complex hyperdiploid karyotype with several identified (nos. 1, 11, and 22) and unidentified supernumerary chromosomes in addition to the 5q–. In cases 5, 6, and 8, all evaluable cells featured both the 5q– and other abnormalities: −7, 11q−, +21, t(3;13). In case 9, several superimposed abnormalities were found, but it was not possible to identify all of them.

In the patient with polycythemia vera (case 10), the development of the chromosome abnormalities followed a different pattern. At the time of diagnosis, all examined cells belonged to an abnormal clone with a 47,XY,20q− karyotype. Three years later, 2 minor clones were identified, both without the original 1p− marker: 46,XY,20q− (18%) and 47,XY,+9,20q− (8%), respectively. In the last study, when the patient had entered a phase of progressive disease, some of the previously 47,XY,+1p−,20q− cells were found to have acquired a 5q– deletion also. This last subclone made up one-third of the original clone.

Structurally abnormal marker chromosomes other than the 5q– were found in 4 patients (case 2, 6, 8, and 10) (Table 3). The markers observed in case 10 were discussed previously. The other markers are shown in Fig. 2. In case 6, a second deletion was found, constituting a loss of most of the long arm of chromosome 11, del(11) (q14?). In case 2, a reciprocal translocation was present between chromosomes 9 and 11. The exchange of material had occurred in or very near the centromere region of both chromosomes, i.e., t(9;11) (9p11;p9q11q). In case 8, a short segment
Table 4. Cytogenetic Pattern and Clinical Diagnosis in 69 Patients With the 5q− Deletion
(Present Series [PS] Plus 59 Cases From the Literature)

<table>
<thead>
<tr>
<th>Refractory Anemia</th>
<th>Preleukemic Syndrome</th>
<th>Secondary Leukemia</th>
<th>Myeloproliferative Disorders</th>
<th>Lymphoproliferative Disorders</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Development of Leukemia</td>
<td>Without Development of Leukemia</td>
<td>Development of Leukemia</td>
<td>Development of Leukemia</td>
<td>Development of Leukemia</td>
<td>References</td>
</tr>
<tr>
<td>(1) 5q− as single abnormality</td>
<td>15</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>(2) 5q− as single initial abnormality but later development of other abnormalities</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>Case 1, 2 PS/case 4 PS, 34/35, case 3 PS</td>
</tr>
<tr>
<td>(3) 5q− plus additional abnormalities</td>
<td>5</td>
<td>2</td>
<td>19</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>(4) 5q− as a secondary event</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td>Case 10 PS, 24</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>5</td>
<td>21</td>
<td>11</td>
<td>7</td>
</tr>
</tbody>
</table>

(q21–q27?) from the long arm of chromosome 3 was translocated to chromosome 13, and probably inserted into the proximal part of the long arm.

DISCUSSION
A recent survey of the literature has yielded a total of 59 patients with the 5q− deletion, reported in sufficient clinical and cytogenetic detail. Most of them are summarized by Sandberg,16 but since that publication a number of further cases have been added.17-27,46 From the gathered information, it now seems quite obvious that the 5q− deletion is not limited to patients with refractory anemia or a preleukemic syndrome. Most cases have had either preleukemia (39%) or leukemia (46%), but myeloproliferative (polycythemia vera, myelofibrosis) and lymphoproliferative (myeloma, lymphoma) disorders are also represented. In Table 4, the 10 patients from the present series and the evaluable cases from the literature are summarized and tentatively subdivided according to the cytogenetic pattern into 4 groups:

(1) 5q− as single abnormality. This group is almost exclusively made up of the initial 5 patients with the “5q− syndrome,” reported by Sokal et al.8 and 11 further cases from the literature that presented with refractory anemia or preleukemia.19-21,28-30 A single 5q− deletion was also observed in 4 leukemic patients18,20,31-32 and in one case of thrombocythemia.33 It is worth noting that at least 2 of the leukemic patients passed through a preleukemic phase.20,31

(2) 5q− as single initial abnormality, but later development of other abnormalities. This category includes cases 1–4 from the present series, one of the patients reported by Verhest et al.,34 and a case of secondary leukemia in a myeloma patient.35 In 3 of our patients (cases 1–3: preleukemic syndrome, refractory anemia, myeloproliferative syndrome), new clonal abnormalities were observed in cells without the initial 5q− deletion. Case 4 in the present series and one further patient34 were followed cytogenetically through preleukemia and leukemia, and in both cases the development of leukemia was accompanied by the appearance of additional abnormalities, −5 and +9, respectively. In the myeloma patient reported by Liang et al.,35 the bone marrow during leukemia was dominated by a hyperdiploid clone with multiple abnormalities besides the 5q− (+1, +6, −7, +10, +21).

(3) 5q− plus additional abnormalities. Under this heading are cases 5–9 of the present series and 34 cases from the literature.17,18,22-24,36,27,32,33,46-46 most of them with multiple anomalies in addition to the 5q−. Thirty-one cases (79%) had a malignant disorder, either leukemia or lymphoma. Case 7 in the present series and a case reported by Streuli et al.23 had preleukemia of the RAEB type,14 which transformed into overt leukemia within a year. Only 5 other patients with refractory anemia or preleukemia belong to this category: case 6 in the present series and 4 previously published cases.34,26,33,36 The abnormal clone in 3 of these latter patients contained just one further structural abnormality besides the 5q− (11q−, 21q−, 22q+). In the case reported by Knuutila et al.,26 other abnormal clones were present besides the 5q− clone, as in our cases 1–3 (Table 3).

In conclusion, it can be stated that when the 5q− deletion was detected in a preleukemic condition, it usually appeared as a single abnormality (74%), while...
during overt leukemia it was accompanied regularly by other abnormalities (88%).

(4) 5q- as a secondary event. Four patients with polycythemia vera and 5q- deletions have been reported: 3 cases by Van Den Berghe et al.24 and case 10 in the present series. In all cases, the 5q- positive clone appeared late in a marrow that had been previously cytogenetically examined and found to be normal (2 cases) or abnormal (2 cases). The primary karyotypes in the latter patients were 47,XY,+1p,20q- and 47,XY,1q-,t (1;18), +9,20q-+/47,XY,+9,11q-,20q-, respectively. The 5q- abnormality occurred in all cases simultaneously with a transformation into a "spent phase" or myelofibrotic stage, but without the development of overt leukemia. The patients had been treated with phlebotomies alone (case 10, present series), 32P, or busulfan.24

It might also be profitable to subdivide the 5q- cases according to the size of the deletion or the estimated break point. However, this discussion is hampered by the fact that for many patients, especially most of the leukemic ones, sufficient cytogenetic details have not been reported. Eight patients in the present series had the loss of a central portion of the long arm of chromosome 5 in common, i.e., region 5q15-5q31. In at least 4 of them, the deletion was interpreted as interstitial (proximal break in q13-15, distal break in q31-34). In most previously reported cases, the deletions seem to have had an appearance similar to our cases 1-7 and have been described either as terminal (q15,26 q22,20,35,41) or more frequently as interstitial (q12q31,31,34,37 q12q23,23). A distinction should probably be made between this type of 5q- deletion, which results in a loss of at least the region 5q22-5q23 and is apparently characteristic for almost all of the preleukemic patients, and terminal deletions with a more distal breakpoint. Abnormalities of this latter type (with a break in q31, Fig. 2) were present in cases 9 and 10 of the present series (leukemia, polycythemia vera). A deletion with a similar appearance was described by Mark et al.42 and seemed also to be present in one of the cases reported by Mahmood et al.21

In 2 of the leukemic patients in the present series (cases 4 and 8), the leukemia might have been of a secondary nature. Case 4 had a long history of exposure to organic solvents, and case 8 had a multiple myeloma treated with melphalan for more than 4 yr. Recently, loss of chromosomes 5 and/or 7 has been described as a cytogenetic finding, typical for secondary leukemia.18,47 In both our patients, involvement of these chromosomes was noted in addition to the 5q- deletions. In case 4, a small subclone of -5 cells was observed after the development of leukemia (Table 3). This development has not previously been described in a 5q- patient. However, it should be noted that only 3 cells with -5 were found out of a total of 28 scorable cells, and an artifact cannot be completely ruled out. In the second patient (case 8), two 5q- positive clones were present, both of which lacked chromosome 7.

The available data give some support to the hypothesis that the 5q- anomaly primarily appears as a single abnormality in certain patients with "the preleukemic syndrome" (Table 4). During the course from preleukemia to leukemia, additional abnormalities may develop, usually as the result of clonal evolution in cells already marked by the 5q-. When examined during full-blown leukemia, the bone marrow often contains multiple, sometimes superimposed, abnormalities besides the deletion. At present, there is no evidence supporting the assumption that preleukemic phase always precedes the development of 5q- positive acute leukemia. Only 3 patients have been followed with cytogenetic examinations through both preleukemia and leukemia: case 4 in the present series and 2 other cases.20,24 In all of them, the 5q- clone persisted during the leukemic phase, and in 2 cases further abnormalities were added when leukemia supervened. On the other hand, even if it seems without doubt that some 5q- cases eventually terminate in leukemia, this may not be the outcome in all. Patients 1-3 in this series have been followed for 3, 7, and 6 yr, respectively, without any change of the clinical course. In this respect the 5q- may be similar to certain other "nonspecific" chromosome abnormalities, like trisomy 8 and 9 and the 20q- deletion, which in some patients may be followed for many years without signs of clonal evolution or the development of leukemia.

Common for all patients (except perhaps case 7) in the present series was a marked disturbance of the megakaryopoiesis. Three cases had thrombocytosis, and an increased number of megakaryocytes in the bone marrow with a large proportion of small megakaryocytes with few nuclear lobes was noted in all categories of patients (preleukemic, leukemic, myeloproliferative) (Table 2). Such a megakaryocytic dyscrasia was presented as a characteristic feature of the 5 patients in the original report of the "5q- syndrome" by Sokal et al.8 and has subsequently been described in other cases of 5q- refractory anemia or preleukemia.21,25 However, for most of the reported 5q- patients, sufficient details regarding platelet level or megakaryopoiesis are not available.

Megakaryocytic abnormalities have previously been well documented both in leukemia84 and in preleukemia.49,51 We are impressed by the degree of mega-

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karyocytic involvement in the present series of 5q– patients, but even if the discussion is limited to preleukemia, we hesitate to state that a specific association exists between the 5q– and a disturbed megakaryopoiesis: our cytogenetically examined patients were not derived from an unselected series, it is not known if a megakaryocytic dyscrasia is common for all cases, and it is not known if, or to what extent, 5q– deletions may occur in the absence of megakaryocytic disturbances. It is possible that 5q– cases merely constitute a subgroup of preleukemic patients who all have a disturbed megakaryopoiesis. In order to fully elucidate the problem it would be necessary to combine quantitative and ultrastructural studies of the megakaryopoiesis with cytogenetic examinations in unbiased samples of preleukemia and leukemia.

REFERENCES


37. Oshimura M, Hayata I, Kakati S, Sandberg AA: Chromo-
THE 5q– DELETION

51. Maldonado JE: The ultrastructure of platelets in refractory anaemia (Preleukemia) and myelomonocytic leukemia. Series Haematol 8:101–125, 1975
On the 5q- deletion: clinical and cytogenetic observations in ten patients and review of the literature

B Swolin, A Weinfeld, B Ridell, J Waldenstrom and J Westin

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