to store iron, although hemoglobin values were on the borderline of normal. The number of HFR decreased, but not significantly. The mean values of serum ferritin in the first group of patients was 194.9±124.8 ng/mL, while it was 1091.1±733 ng/mL in the second group.

We believe that the improvement shown in hematologic and reticulocyte parameters in the group of younger patients with normal serum ferritin supports the hypothesis of effectiveness of enzyme replacement therapy.5,6 The reason for the high levels of serum ferritin in the second group of patients remains to be clarified, but evidence that these levels occur in patients who can no longer be considered pediatric, and who have slight hepatosplenomegaly, suggests that these may be due to spleen damage from myelo-atrophic-like lipid infiltration. In this second group, it is probable that the dosage used in therapy (30 u/kg/day) was not sufficient for adult subjects, whose storage was greater. Accordingly, for some of these patients, we suggest an increase in the dosage of enzyme replacement therapy and, if necessary, iron chelation therapy with desferrioxamine.

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Key words
Gaucher’s disease, enzyme replacement therapy.

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References

P53 overexpression in refractory anemia. An immunohistochemical analysis of bone marrow biopsies

Sir,

Genetic abnormalities are common in myelodysplasia (MDS) but molecular mechanisms underlying the latter’s genetics and evolution are still largely unknown.1 The characterization of p53 tumor suppressor gene in MDS patients revealed alterations in 5% to 10% of cases2-6 which were almost exclusively seen in more advanced phenotypes.

Bone marrow biopsies obtained at diagnosis from 19 patients with MDS in refractory anemia (RA) phase were immunohistochemically studied. The patients’ age at diagnosis was in the range from 20 to 82 years. Nine of the patients were men (47.4%). Using a technique for antigen retrieval based on microwave oven heating and an alkaline phosphatase anti-alkaline phosphatase complex, p53 overexpression was detected in two cases (10.5%). P53 positive cells constituted 36% and 39% of total bone marrow cells (Figure 1). Five patients (26%) evolved to a more advanced subtype or overt acute leukemia, including the two cases with abnormal p53 expression (Table 1). Time to progression was 3 and 4 months for the p53-positive patients and 48, 11 and 30 months for the p53-negative patients. RA cases that progressed to a more aggressive subtype later exhibited a significantly higher frequency of p53 overexpression (2/5-40%) than cases that did not transform (0/14-0%) (p<0.001).

Immunohistochemical analysis may often tell us more about the functional status of the p53 control pathway than DNA sequencing does.7 Although mutations of p53 gene can be inferred from immunohistochemical detection of accumulated mutant protein, there is not an absolute correlation. In general, detection by molecular methods yields lower frequencies of abnormality than immunostaining.8 Possible reasons include: a) a minor subclone, below the detection level of single strand conformation polymorphism analysis, but detected by immunologic techniques, had acquired a mutation; b) non-muta-

Table 1. Summary of patients with disease progression and correlation to p53 status at initial diagnosis.

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex/ Age</th>
<th>Disease progression</th>
<th>p53 status*</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>M/22</td>
<td>RAEB-</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>F/20</td>
<td>RAEB-</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>M/35</td>
<td>RAEB</td>
<td>-</td>
</tr>
<tr>
<td>9</td>
<td>M/63</td>
<td>RAEB</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>M/68</td>
<td>AML</td>
<td>+</td>
</tr>
</tbody>
</table>

* + ≥ 5% of positive cells; - = < 5% of positive cells
tional stabilization of the protein which may also abolish its function; c) overexpression of wild-type protein in response to spontaneous genetic errors occurring at a higher frequency in neoplastic tissue; d) the effect of antigen retrieval techniques which can alter detection thresholds; e) mutations occur outside the exons studied.

Several reports have described that p53 alterations are not observed in more benign MDS cases.2-6 However, this study, in keeping with a study done by Kitagawa et al.9 revealed two RA cases showing p53 overexpression suggesting that p53 abnormality may not be a terminal genetic event during leukemia development. To the best of our knowledge only one other study has described p53 alteration in the RA phase.10 The presence of DNA from normal cells in less advanced subtypes is likely to affect the sensitivity of the mutation detection and may underestimate the rate of p53 mutation in RA phase.

Taking into account the shorter interval between RA phase and progression, p53 overexpression may have contributed to the pathogenetic process in the progression of MDS in our cases. However, additional and more extended studies are necessary to determine the genetic basis for this immunoreactivity and to clarify the prognostic value of such findings.

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References

A complex immunodeficiency. Idiopathic CD4+ T-lymphocytopenia and hypogammaglobulinemia associated with HHV8 infection, Kaposi’s sarcoma and gastric cancer

Sir,

We report a case of idiopathic CD4+ T-lymphocytopenia (ICL) associated with hypogammaglobulinemia in a 70-year-old woman. She developed Kaposi’s sarcoma (KS) and her mononuclear cells were found to be positive for Herpes virus type 8 (HHV8). In 1997 she developed gastric cancer and died from septic shock.

At the beginning of 1990 unusual cases of CD4+ T-lymphocytopenia in the absence of human immunodeficiency virus (HIV) infection were reported.1,2 In 1993 the CDC defined the criteria for a new syndrome: ICL. The criteria are low CD4+ T-lymphocytes (less than 300/µL or below 20% of the total lymphocyte count), no serologic evidence of HIV infection and no defined immunodeficiency diseases or therapy associated with T-cell depletion.1

In 1994 a 70-year-old woman with hypertension and herpes zoster virus infection was admitted to our section because of fever, skin abscesses due to Serrata marcescens and angiomatous abscesses on the left leg. There was no epidemiology suggestive of HIV