concentrations tended to be higher in patients with cardiac symptoms as shown in this case, we propose that tacrolimus could be the causative agent of this patient’s myocardial ischemia, and clinicians should be aware of this potential toxic manifestation. The patient’s ATIII activity was decreased below normal when the attack occurred. There are reports that the ATIII level decreases during BMT, which could cause a hypercoagulable state and result in a wide spectrum of thrombotic complications. But in this case, because coronary angiography revealed no organic stenosis, microthrombi formation due to low ATIII activity would be unlikely as the cause of this event.

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References

To the editor:

Differences between refractory anemia with excess blasts in transformation and acute myeloid leukemia

The recently proposed World Health Organization (WHO) classification of hematologic malignancies attempted to integrate morphologic, clinical, immunophenotypic, and genetic features in defining disease entities. One of the major changes proposed by this classification is to lower the blast count for acute myeloid leukemia (AML) from 30% to 20%, thereby eliminating the pre-classification is to lower the blast count for acute myeloid leukemia entities. One of the major changes proposed by this logic, clinical, immunophenotypic, and genetic features in defining cation of hematologic malignancies attempted to integrate morpho-

Figure 1. Box-plot comparing caspase 3 activity between various diseases. The indicated P reflects the Kruskal-Wallis test in comparing the 3 groups.

Table 1. Comparison of RAEB-T with AML

<table>
<thead>
<tr>
<th></th>
<th>RAEB-T median (range)</th>
<th>AML median (range)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caspase 3 activity*</td>
<td>7.87 (0-26)</td>
<td>1.94 (0-26)</td>
<td>.0001</td>
</tr>
<tr>
<td>PCNA*</td>
<td>3.35 (.98-7.88)</td>
<td>1.92 (.74-17.28)</td>
<td>.008</td>
</tr>
<tr>
<td>Age</td>
<td>61.5 (19-84)</td>
<td>59.5 (16-87)</td>
<td>NS</td>
</tr>
<tr>
<td>AHD</td>
<td>1 (0-1000)</td>
<td>0 (0-168)</td>
<td>NS</td>
</tr>
<tr>
<td>B2M</td>
<td>2.4 (1-8.10)</td>
<td>2.6 (0-31)</td>
<td>NS</td>
</tr>
<tr>
<td>PLT</td>
<td>38.5 (1-471)</td>
<td>49 (3-2292)</td>
<td>.017</td>
</tr>
<tr>
<td>HGB</td>
<td>7.7 (3.6-15.1)</td>
<td>7.8 (2.8-15)</td>
<td>NS</td>
</tr>
<tr>
<td>VEGF*</td>
<td>4 (1-15)</td>
<td>3 (5-15)</td>
<td>.04</td>
</tr>
<tr>
<td>BM cellularity</td>
<td>65 (5-100)</td>
<td>75 (5-100)</td>
<td>.05</td>
</tr>
<tr>
<td>Poor cytogenetics</td>
<td>50%</td>
<td>35%</td>
<td>.001</td>
</tr>
<tr>
<td>Therapy-related</td>
<td>27%</td>
<td>15%</td>
<td>.011</td>
</tr>
</tbody>
</table>

*The values of caspase 3 activity, PCNA, and VEGF represent folds of the mean level observed in 12 normal control bone marrows, which is assigned a value of 1.
M. D. Anderson Cancer Center from the beginning of 1994 to the end of 1998, including 142 patients with RAEB-T, 106 patients with “other MDS” (RA, RAEB, and RARS), and 514 patients with AML.

MDS is distinguished from AML by a significant increase in apoptosis, as assessed by caspase 3 activity measured using a tetrapeptide Ac-DEVD-pNA (Calbiochem, San Diego, CA). When we compared caspase 3 activity in RAEB-T with that in AML, there was significantly higher activity in RAEB-T (P < 0.0001). By contrast, there was no significant difference in caspase 3 activity between other MDS and RAEB-T (Figure 1).

Of note, there was no overlap between AML and RAEB-T or other MDS in caspase 3 activity, whereas there was complete overlap between RAEB-T and other MDS. In addition, PCNA levels, which reflect proliferation, were significantly higher in RAEB-T than in AML (Table 1) (P = 0.008). By contrast, there was no significant difference between MDS and RAEB-T in PCNA levels (Table 2). Intracellular vascular endothelial growth factor (VEGF) levels in RAEB-T, which we reported to have prognostic value in AML, were significantly different from those in AML (P = 0.04) but not from those in other MDS (Figure 2, Tables 1 and 2).

Upon examining other clinical characteristics as shown in Tables 1 and 2, clearly there is significant difference between AML and RAEB-T in the presence of antecedent hematologic diseases (AHD), platelet count, bone marrow cellularity, and the incidence of poor-prognosis cytogenetics (Table 1). In addition, RAEB-T disease was significantly more likely to be therapy-related than AML. By contrast, comparison of RAEB-T with MDS shows no difference between the 2 groups in any of the clinical parameters, except for AHD and bone marrow cellularity. In fact, as shown in Figure 3, bone marrow cellularity in RAEB-T is lower than that in other MDS and AML.

The data presented here suggest that biologically RAEB-T is more likely to be an advanced stage of MDS and that it appears different from AML. Of course, there are other biologic characteristics that we have not examined. Furthermore, it is possible that high caspase 3 activity is dependent not so much on RAEB-T/other MDS grouping as on other features. Nevertheless, we believe our data suggest that there is sufficient biologic distinction between AML and RAEB-T to warrant retaining the latter as a separate entity.

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References


