CORRESPONDENCE

THE CLINICAL EVALUATION OF HAIRY CELL LEUKEMIA

To the Editor:

It seems to be well established by now that hairy cell leukemia (HCL) patients in apparent complete remission may harbor residual hairy cells in their bone marrow demonstrable only by immunohistologic and not by routine morphologic methods. Recently, Pangalis et al and Catovsky et al reported splenic infiltration with hairy cells in HCL patients treated with interferon-α2b who before splenectomy were found to have complete remission according to the criteria established during the Second International Hairy Cell Leukaemia Conference. These criteria do not include bone marrow immunohistology. Neither have immunohistochemical studies been reported in patients in apparent complete remission induced by 2-chloro-deoxyadenosine.

We completely agree with Pangalis et al that the present criteria of complete remission in HCL are not satisfactory. The finding of complete remission is greatly influenced by the sensitivity of the methods applied to detect residual disease (e.g., immunohistology, molecular biology). On the other hand, HCL patients may harbor the disease indolently for many years without therapy and progression-free survival is possible despite residual hairy cells after interferon-α2 therapy.

These facts led us to suggest functional criteria for the clinical evaluation of HCL patients. According to our suggestion, patients with nonsymptomatic and stable disease should be distinguished from those with disease-related symptoms and/or progressive disease. Criteria of nonsymptomatic disease are no recurrent infections, no symptoms of anemia or transfusion requirements, no symptoms caused by organomegaly, and no constitutional symptoms. Criteria of stable disease are stable peripheral blood counts (hemoglobin, granulocytes, platelets) over the previous 3 months, alterations within the normal range being neglected. The functional criteria for staging and treatment of HCL enable us to distinguish patients with nonsymptomatic and stable disease not requiring therapy from those with symptomatic and/or progressive disease where treatment is necessary.

Certainly the clinical course of the patients reported by Pangalis et al and Catovsky et al is of major interest as HCL is likely to originate from the spleen and the spleen is always involved in this disease (while in exceptional cases the bone marrow was found not to be involved). The time elapsed since splenectomy could allow some conclusions by now, as progression of the disease was shown to occur in 45% of HCL patients within 25.4 months (range, 2.5 to 41 months) after completion of interferon-α2b treatment.

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REFERENCES


RESPONSE

We appreciate the comments made and the questions raised by Drs Demeter and Porzsolt regarding our previous report on hairy cell leukemia (HCL) patients splenectomized while in complete remission after 12 months of α2-interferon (IFN) therapy. In this study it was demonstrated for the first time that in all spleens removed easily recognizable red pulp disease was present. No evidence of bone marrow disease was found in any of our patients at the time of splenectomy and this was confirmed not only
morpologically but also by cytochemistry and immunocytochemistry. Thus, tartrate-resistant acid phosphatase stain and peroxidase-antiperoxidase immunocytochemistry using the CD20 (L26) antibody performed on bone marrow smears and sections, respectively, were unable to demonstrate positive cells. One may argue, however, as Drs Demeter and Porzsolt do, that with more sensitive and sophisticated methods (such as molecular biology) rare hairy cells could be identified in the bone marrow. Nevertheless, the question still remains why massive morphologically easily recognizable splenic red pulp disease was present in every patient (Fig 1), while there was no clearly evident bone marrow disease, despite the fact that at diagnosis and before α-IFN therapy all patients had extensive diffuse bone marrow infiltration.5,6 It appears that our findings strongly support the notion that HCL may be originated in the spleen.

Regarding the criteria suggested by Drs Demeter and Porzsolt, these seem to be applicable in a high number of HCL patients, but not in our patients. In fact, two of our patients who relapsed 6 and 36 months after splenectomy had no detectable bone marrow disease at the completion of 12 months of α-IFN therapy, their spleen harboring the disease had been removed and, therefore, according to their criteria, they should be considered as having nonsymptomatic disease. Nevertheless, they progressed in a rather short period of time, although they had no recurrent infections, no symptoms of anemia or transfusion requirement, no symptoms caused by organomegaly, and no constitutional symptoms.5,6

Finally, the follow-up information of our patients at 18 months indicated that only one patient relapsed,5 while during a recent reevaluation a second patient was also relapsed 36 months postsplenectomy. The remaining four patients are still without evidence of disease 31, 36, 37, and 36 months postsplenectomy. Detailed information during a current reevaluation of our patients is given in Table 1. Despite the fact that the number of patients under discussion is small, disease progression was observed in two of six (33%) so far and this progression occurred within 28.6 months (range, 6 to 37 months) postsplenectomy. This progression appears to be slower as compared with patients placed on follow-up observation after discontinuation of α-IFN treatment.5 Based on our findings, we believe that splenectomy was beneficial for our patients. Of course, to document whether any of them is going to be cured with this therapeutic approach, much longer follow-up is required.

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Table 1. HCL: Results of Various Clinical and Laboratory Findings

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex</th>
<th>Age</th>
<th>Months Post-splenectomy</th>
<th>Hb (g/dL)</th>
<th>Polys (×10⁹/L)</th>
<th>PLT (×10⁹/L)</th>
<th>HC in Bone Marrow (%)</th>
<th>s-IL2R* (U/mL)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>46</td>
<td>37</td>
<td>14.1/15.2</td>
<td>2.3/3.2</td>
<td>107/280</td>
<td>0/0</td>
<td>0/0</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>37</td>
<td>31</td>
<td>13.1/14.1</td>
<td>1.3/3.5</td>
<td>107/320</td>
<td>0.0/0.0</td>
<td>0/0</td>
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<tr>
<td>3</td>
<td>M</td>
<td>47</td>
<td>6</td>
<td>15/15.1</td>
<td>1.5/2.9</td>
<td>110/300</td>
<td>0.1/0.5</td>
<td>0/0</td>
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<tr>
<td>4</td>
<td>M</td>
<td>52</td>
<td>36</td>
<td>14/15.0</td>
<td>2.1/3.2</td>
<td>120/250</td>
<td>0.05/0.0</td>
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</tr>
<tr>
<td>5</td>
<td>M</td>
<td>45</td>
<td>36</td>
<td>13.2/14.8</td>
<td>1.4/3.9</td>
<td>127/240</td>
<td>0.1/0.25</td>
<td>0/0</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>54</td>
<td>36</td>
<td>12.1/13.5</td>
<td>2.1/4.1</td>
<td>160/350</td>
<td>0.05/0.0</td>
<td>0/0</td>
</tr>
</tbody>
</table>

The first figure is that at 12 months after α-IFN administration and splenectomy; the second figure is that postsplenectomy in months as indicated in column 4.

Abbreviations: Hb, hemoglobin; Polys, polymorphonuclear neutrophils; HC, hairy cells; PLT, platelets; s-IL2R, soluble interleukin-2 receptors.

*Control values: 524.5 ± 238 U/mL.
REFERENCES

The clinical evaluation of hairy cell leukemia [letter; comment]

J Demeter and F Porzsolt