CONCISE REPORT

Chlorambucil Therapy in Hairy Cell Leukemia: Effects on Lipid Composition and Lymphocyte Subpopulations

By Robert Krigel, Leonard F. Liebes, Edward Pelle, and Robert Silber

Two patients with progressive hairy cell leukemia following splenectomy were treated with low-dose daily chlorambucil. Both had an objective hematologic response as determined by a return to normal hematocrit and platelet count. This was also reflected in the mononuclear cell fraction by the normalization of cholesterol content, cholesterol/phospholipid ratio, and the lymphocyte subpopulations. This article confirms previous reports on the efficacy of chlorambucil in this setting and describes some morphological, immunologic, and biochemical concomitant events.

RESULTS AND DISCUSSION

Case 1 (See Fig. 1)

The patient is a 54-yr-old white male who was found to have HCL 4 yr ago on a routine complete blood count. At that time his white blood cell count (WBC) was 6.0 x 10^9/µl. Confirmatory bone marrow biopsy and TRAP were done. One year later, the hematocrit (Hct) decreased to 18% and the platelet count was 66% x 10^9/µl. A splenectomy was performed with a subsequent rise in Hct to 27% and platelet count to 113 x 10^9/µl. However, within 1 yr, the Hct had decreased to 16%, platelet count had decreased to 88 x 10^9/µl, and the WBC had increased to 46 x 10^9/µl. The patient was treated with chlorambucil, 4 mg/day. The dosage was reduced to 2 mg/day within 1 mo. Three months after initiating treatment, the chlorambucil was discontinued. The Hct was 38%, WBC 2.0 x 10^9/µl, and platelet count 235 x 10^9/µl. Chlorambucil and C/PL ratio returned to normal (Table 1). T-cell and B-cell lymphocyte percentages had also returned to normal (Table 1). Cell sizing confirmed the decrease in HC. In May 1981, the patient was hospitalized because of fever and a pulmonary infiltrate. Although no pathogen was cultured, he defervesced on clindamycin and gentamicin. During the hospitalization, the WBC increased to 5.0 x 10^9/µl (77% granulocytes). Eighteen months after the discontinuation of chemotherapy, the hemogram was as follows: Hct 45%, WBC 3.5 x 10^9/µl, and platelet count 225 x 10^9/µl. Rare HC persist on the peripheral smear.

Case 2 (See Fig. 1)

The patient is a 65-yr-old white male who was found to have an elevated WBC 3.5 yr ago. The diagnosis of HCL was made upon referral to this institution 6 mo later when bone marrow biopsy and TRAP confirmed the diagnosis suggested on peripheral smear. At

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that time, the Hct was 34%, WBC $9 \times 10^3/\mu l$, and platelet count $66 \times 10^3/\mu l$. A splenectomy was performed 1 yr later because of progressive splenomegaly, anemia, and thrombocytopenia. Following surgery, the Hct increased to 38% and the platelet count rose to $171 \times 10^3/\mu l$, but within 2 mo, the WBC had increased to $100 \times 10^3/\mu l$. The patient was treated with chlorambucil, 4 mg/day, which was decreased to 2 mg/day 6 mo later. Cholesterol, C/PL ratio, and T-cell percentages have returned to normal (Table 1) and EAC were 1%. Cell sizing shows that HC are now a very minor component when compared to the pretreatment values (Fig. 2). Four months later, with the patient still on treatment with chlorambucil, the Hct was 43%, WBC $5.7 \times 10^3/\mu l$ (28% granulocytes), and platelet count $308 \times 10^3/\mu l$.

Two patients with HCL and progressive disease following splenectomy have been treated with low-dose daily chlorambucil. Both cases showed an excellent response. This confirms the efficacy of this drug in the treatment of this disorder.5,6

Cell sizing accurately reflects the percentage of HC on peripheral smear.13 Chlorambucil appears to selec-

Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Cholesterol ($\mu$ mole/10^9 Cells)</th>
<th>C/PL†</th>
<th>T Cell¶</th>
<th>B Cell¶</th>
</tr>
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<tbody>
<tr>
<td>HC</td>
<td>$4.7 \pm 1.5$‡§</td>
<td>0.60 ± 0.09§</td>
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<td>Monocyte</td>
<td>$5.8 \pm 2.1$</td>
<td>0.59 ± 0.06§</td>
<td></td>
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<tr>
<td>Lymphocyte</td>
<td>$2.8 \pm 0.7$</td>
<td>0.50 ± 0.07§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient 1</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Postsplenectomy</td>
<td>$7.1 \pm 2.2$‡</td>
<td>0.60 ± 0.09 (7)</td>
<td>16.1</td>
<td>6.8</td>
</tr>
<tr>
<td>Day 20 CLB rx*</td>
<td>$2.7$</td>
<td>0.42</td>
<td></td>
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</tr>
<tr>
<td>Day 60 CLB rx</td>
<td>$3.2$</td>
<td>0.50</td>
<td>66.2</td>
<td>13.8</td>
</tr>
<tr>
<td>Patient 2</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Presplenectomy</td>
<td>$5.2 \pm 0.6$‡</td>
<td>0.60 ± 0.11 (8)</td>
<td>23.4</td>
<td>5.8</td>
</tr>
<tr>
<td>Postsplenectomy</td>
<td>$6.0$</td>
<td>0.64</td>
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<tr>
<td>Day 80 CLB rx</td>
<td>$4.1$</td>
<td>0.46</td>
<td>46.7</td>
<td>1.0</td>
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<tr>
<td>Day 200 CLB rx</td>
<td>$2.3$</td>
<td>0.44</td>
<td>59.6</td>
<td>0.9</td>
</tr>
</tbody>
</table>

*CLB rx, chlorambucil therapy.
†Cholesterol/phospholipid ratio.
‡Mean ± SD.
§Previously published data.
¶Number in parenthesis is the number of samples.
\(\text{T Cell} \) Percent monocyte-depleted mononuclear cells.
chlorambucil treatment induces a return to normal Hct and platelet count (Fig. 2). Although the WBC remains somewhat low, granulocyte reserve may be adequate, as seen in patient 1 during an episode of pneumonia. Low-dose daily chlorambucil appeared effective in postsplenectomy HCL patients with progressive disease. Further studies are needed on the efficacy of this agent prior to splenectomy.

REFERENCES

8. Shevach EM, Herberman R, Frank MM, Green I: Receptors
EFFECT OF CHLORAMBUCIL ON HAIRY CELLS


Chlorambucil therapy in hairy cell leukemia: effects on lipid composition and lymphocyte subpopulations

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