B-cell prolymphocytic leukaemia —
clinical and haematological features

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Summary

Prolymphocytic leukaemia is an unusual but distinctive variant of chronic lymphocytic leukaemia which generally responds poorly to chemotherapy. Four cases are described to illustrate typical clinical and haematological features and to emphasise the unsatisfactory outcome with combination chemotherapy, radiotherapy and plasma exchange in 3 patients, and to draw attention to the prolonged disease control which followed splenectomy in the fourth. These observations illustrate the relative ease with which the diagnosis can be made and also the difficulties in management, which requires exploration of alternative treatment options.

Patients and methods

The presenting clinical and haematological findings in 4 patients with prolymphocytic leukaemia are summarised in Table I. A full blood count and biochemical profile, together with bone marrow aspiration and trephine biopsy, electron microscopy and determination of cell membrane surface markers using a standardised library of monoclonal antibodies were carried out on all patients when first seen.

Results (Table I)

Clinical. The patients were aged between 47 and 73 years, and all had marked splenomegaly with fatigue and loss of weight and appetite. Lymphadenopathy was insignificant.

Haematological. Normochromic and normocytic anaemia with thrombocytopenia was the common finding and total white cell counts above 100 x 10⁹/l were present in only 2 of the 4 patients. All showed classic prolymphocytic morphology in the peripheral blood and on ultrastructural examination. Bone marrow aspiration and trephine biopsy revealed more than 80% of the same cells in all patients, ranging from extensive aggregate to diffuse interstitial patterns.

Phenotypically (Table II), the tumours were of B-cell lineage, all expressing IgM and, when tested for, IgD in addition. Only K-light chains with intense surface staining were present and this contrasts with the lesser degree of fluorescence usually seen with classic chronic lymphocytic leukaemia, being more consistent with the pattern present in lymphoma. No T-cell variants were present in this series.

Therapy (Table III) varied, with single and combination chemotherapy being ineffective, as was total body irradiation and radiotherapy to the spleen. Intensive leukapheresis transiently reduced the white cell count, but this was of short duration. Splenectomy could not be undertaken in 1 patient because of severe respiratory disease, but splenectomy resulted in good stable disease control in a second. In the remaining 2 patients removal of the spleen was technically successful, but the operation had no effect on response to chemotherapy, whether this was given before or after surgery.

Discussion

Clinically and haematologically, the 4 cases described fulfil the criteria which are now accepted for the diagnosis of B-cell prolymphocytic leukaemia. Thus, marked to massive symptomatic splenomegaly, paucity of superficial lymphadenopathy, high white cell count with characteristic light and ultrastructural morphology, together with B-cell phenotype using appropriate cell membrane surface markers were present in all; no T-cell variants were present. It has been suggested that lymphadenopathy becomes a distinctive feature in some T-cell variants, and while this finding was not present in our cases atypical B-cell types may produce prominent enlargement of peripheral lymph nodes.

The poor overall response to chemotherapy was again evident in our patients with B-cell prolymphocytic leukaemia, with neither chemotherapy nor radiotherapy being effective and an intensive leukapheresis programme having transient value only. Similarly, splenectomy was of limited value in 2 of the 3
patients who underwent surgery, although it resulted in disease stabilisation in 1. It follows that alternative forms of management need to be explored. The use of recombinant α-interferon has precedent in the treatment of hairy-cell leukaemia\(^3\) as well as varying response rates in other B-cell lymphoproliferative disorders, including myeloma that has become refractory to chemotherapy and radiotherapy.\(^4\) Since there are certain phenotypic similarities between hairy-cell leukaemia and B-cell prolymphocytic leukaemia, use of this agent is a realistic therapeutic option. Recently, high-dose chemotherapy and whole-body irradiation, followed by allogeneic bone-marrow transplantation, has been employed in a small number of carefully selected patients with lymphoma.\(^3\) With this precedent, there is no reason why a similar approach should not be explored in B-cell prolymphocytic leukaemia. However, this latter option would be available for a limited number of patients, in view of the age restriction and the need to have a compatible sibling. More recently, the use of autologous bone-marrow transplantation has been advocated to overcome the restrictions of donor availability.\(^6\) In this context, prior therapy to eradicate marrow disease or \textit{ex vivo} purging with monoclonal antibodies to remove residual tumour cells may offer a potentially useful form of treatment.

It is concluded that, while the diagnosis of B-cell prolymphocytic leukaemia can be made with relative ease, management is at present unsatisfactory and although splenectomy may occasionally result in disease control, there is an urgent need to develop alternative treatment strategies.

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TABLE III. SUMMARY OF RESPONSE TO TREATMENT

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Therapy</th>
<th>Response</th>
<th>Survival from diagnosis (wks)</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Splenectomy</td>
<td>Transient decrease in white cell count only</td>
<td>84</td>
<td>Died; increasing tumour bulk, sepsicaemia</td>
</tr>
<tr>
<td>1</td>
<td>CHOP</td>
<td>No response</td>
<td>CNS blasts</td>
<td>78</td>
</tr>
<tr>
<td>2</td>
<td>CHOP</td>
<td>No response</td>
<td>CNS blasts</td>
<td>70+</td>
</tr>
<tr>
<td>2</td>
<td>Radiotherapy to spleen</td>
<td>No response</td>
<td>pneumonia, pulmonary fibrosis</td>
<td>50</td>
</tr>
<tr>
<td>3</td>
<td>Splenectomy + BACOP in CNS after chemotherapy</td>
<td>Minimal response, blasts</td>
<td>57</td>
<td>Alive well, no further therapy</td>
</tr>
<tr>
<td>3</td>
<td>Leucapheresis + BOP + intrathecal methotrexate</td>
<td>Increasing tumour bulk</td>
<td>50</td>
<td>Died; increasing tumour bulk, pneumonia</td>
</tr>
<tr>
<td>4</td>
<td>Total body irradiation</td>
<td>No response</td>
<td>50</td>
<td>Died; increasing tumour bulk, pneumonia</td>
</tr>
<tr>
<td>4</td>
<td>CHOP x 4</td>
<td>Decrease in size of spleen and liver</td>
<td>50</td>
<td>Died; increasing tumour bulk, pneumonia</td>
</tr>
<tr>
<td>4</td>
<td>CTR III + leucapheresis</td>
<td>Increasing tumour bulk, splenomegaly, increased lymphadenopathy</td>
<td>50</td>
<td>Died; increasing tumour bulk, pneumonia</td>
</tr>
</tbody>
</table>

CHOP = cyclophosphamide, hydroxydaunorubicin (Adriamycin), Oncovin and prednisone; BACOP = bleomycin, Adriamycin, cyclophosphamide, Oncovin and prednisone; BOP = bleomycin, Oncovin and prednisone; CTR = Cape Town regimen.

REFERENCES