out relapse.

In CLL patients, the risk of a secondary neoplasm is related to an immunologic deficiency and/or treatment such as chlorambucil. Recent data show that RS cells and CLL cells belong to the same clonal population. RS cells, occurring in CLL or in classical HD, have the same genetic, morphologic and immunophenotypic features.

The good prognosis of HD after CLL distinguishes it from Richter’s syndrome. Indeed it might be considered as a complication of CLL and not only as a coincidental finding. It should be searched for when patients develop signs suggestive of progression or transformation of CLL. Intensive treatment seems to be useful for obtaining CR.

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Key words


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References


Table 1. Characteristics of the 3 patients.

<table>
<thead>
<tr>
<th>Blood lymphocyte immunophenotyping at the diagnosis of CLL</th>
<th>Blood lymphocyte immunophenotyping at the diagnosis of HD</th>
<th>Bone marrow lymphocytic infiltration and no RS cells</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient #1</td>
<td>Lymphocytes: 46.44×10⁹/L</td>
<td>Lymphocytes: 0.3×10⁹/L</td>
<td>Slight lymphocytic infiltration at the diagnosis of HD</td>
</tr>
<tr>
<td>Patient #2</td>
<td>Lymphocytes: 15.6×10⁹/L</td>
<td>Lymphocytes: 2.57×10⁹/L</td>
<td>Nodular infiltration by mature and small lymphocytes without RS cells</td>
</tr>
<tr>
<td>Patient #3</td>
<td>Lymphocytes: 7.8×10⁹/L</td>
<td>Not done</td>
<td>Mild bone marrow infiltration by lymphocytes without RS cells</td>
</tr>
</tbody>
</table>

CD3⁺ large granular lymphocyte leukemia with clonal rearrangement of the γ and β genes of the T-cell receptor

We report the case of a patient with large granular lymphocyte leukemia with a CD3⁺ phenotype and evidence of a monoclonal rearrangement of the TCR γ and β genes. This case seems to show that the proliferation originated from an immature T-thymic progenitor.

Sir,

Large granular lymphocyte (LGL) proliferation of CD3⁺ cells with clonal T-cell receptor (TCR) gene rearrangements is referred to as T-LGL leukemia; LGL proliferations of CD3⁻ cells without TCR gene rearrangements are classified as natural killer (NK)-LGL leukemia.¹⁻²
We report a well documented case of LGL leukemia with unusual biological features. A 46-year old woman was sent to our Hematology Department for study of a stable, isolated chronic severe neutropenia (neutrophils 0.145x10^9/L, lymphocytes 2.904x10^9/L) of 5 years of duration. Morphologic evaluation of the peripheral blood and bone marrow aspiration smears showed the presence of 40% and 13% LGLs, respectively. The LGS in peripheral blood showed expression of CD2, CD7, CD94, CD11c and CD16 and negativity for surface and cytoplasmic CD3, CD5D, CD57, TCRβ, TCRγδ, CD5, CD34 and TdT. Conventional cytogenetics performed on peripheral blood stimulated with PHA showed a normal karyotype. The molecular analysis by polymerase chain reaction and Southern blot revealed rearrangement of the TCRβ and TCRγ genes. To our knowledge, this is the second case reported of TCR gene rearrangement in a patient with CD3– LGL leukemia. Among seven patients with CD3– LGL leukemia analysed for rearrangement of the TCR genes, Hara et al. found one patient with TCRγδ gene rearrangement. Their findings indicate that CD3– LGLs include not only cells belonging to the NK-cell lineage but also precursor cells committed to the T-cell lineage. In the human thymus there are progenitors cells with the capacity to develop into T, NK, and dendritic cells. It has been recently shown that the TCR genes of early thymocyte subpopulations rearrange in an ordered way during human T-cell differentiation; TCRδ rearrange first followed by TCRγ and TCRβ. The rearrangement of the TCRβ gene initiates in T-thymic progenitors.

Taken together, an attractive hypothesis to explain the CD3– phenotype and the TCRγ and TCRβ genes rearrangement in our case would be that the LGL clone may have arisen in a T-thymic progenitor. Since rearrangement of the TCRβ gene strongly suggests T-cell commitment, the cells of this patient may have been arrested at a differentiation stage earlier than the stage of TCRδ gene rearrangement and would have differentiated to CD3+ T-cells bearing the γδ or γδ heterodimer. This concept may be supported by the absence on the cell surface in this patient of CD5, TCRγδ, TCRβ and CD56, which are antigens with lineage-specific and maturation dependent expression, and the positivity for HLA-DR and CD7, antigens that may be associated with immaturity. Overall, our case would support the theory that some cases of CD3– LGL leukemia may represent immature proliferations originating in T-thymic progenitors rather than true peripheral NK neoplasias. Molecular characterization of TCR gene rearrangement status in a greater number of cases of CD3– LGL leukemia would be of great interest to increase our knowledge of this rare pathology.

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Key words
Large granular lymphocyte leukemia, CD3, T-cell receptor gene rearrangement.

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References

Successful treatment of angioimmunoblastic lymphadenopathy with dysproteinemia-type T-cell lymphoma by combined methotrexate and prednisone

Angioimmunoblastic lymphadenopathy with dysproteinemia (AILD)-type T-cell lymphoma has a very poor prognosis in most patients. Here we report a complete clinical response in a patient treated with low-dose oral methotrexate (10 mg/m^2 weekly) in combination with prednisone (15 mg/day) in whom conventional chemotherapy was not effective. This regimen was not associated with