Spectrum of Clonal Large Granular Lymphocytes (LGLs) of αβ T Cells

T-Cell Clones of Undetermined Significance, T-Cell LGL Leukemias, and T-Cell Immunoclones

Timothy P. Singleton, MD,1 Bin Yin, MD, PhD,2 Andinet Teferra, MPH,3 and Jenny Z. Mao, MD3

From the 1Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis; 2Cyrus Tang Hematology Center, Jiangsu Institute of Hematology, the First Affiliated Hospital, Soochow University, Suzhou, China; and 3Hematopathology Laboratory, University of Minnesota Medical Center, Fairview, Minneapolis.

Key Words: Flow cytometry; T-cell large granular lymphocytic leukemia

ABSTRACT

Objectives: Clones of T-cell large granular lymphocytes (LGLTs) were detected by flow cytometry. Disease associations are described.

Methods: Flow cytometry on blood or marrow detected clonal LGLTs by analyzing variable regions of the T-cell receptor β chain.

Results: LGLT clones were detected in 20% (54/264) of tested patients. The clone sizes were less than 2.0 × 109/L in the blood in 73% and less than 10% of marrow space in 94%. Blood counts showed cytopenias. Clinical associations included B-cell clones, myeloid neoplasms, nonneoplastic disorders of blood or marrow, transplants, systemic immune disorders, carcinomas, or hypothyroidism. Twelve patients had LGLT leukemia. Most (76%) had small LGLT clones with limited impact on the clinical management.

Conclusions: Most of the LGLT clones detected by flow cytometry were small and did not change the clinical management. We propose the following terminology: T-cell clones of undetermined significance, LGLT leukemias, and T-cell immunoclones.

T-cell large granular lymphocytic leukemia is defined in the 2008 World Health Organization (WHO) classification as a persistent increase in T-cell large granular lymphocytes (LGLTs) at greater than 2.0 × 109/L in the blood without a known cause.1 Some investigators feel that this is better regarded as a T-cell clonopathy of undetermined significance due to its often indolent clinical course.2,3 With new techniques that can detect T-cell clones at lower levels, the criteria for LGLT leukemia have evolved so that now cases with more than 0.5 × 109/L clonal LGLT cells and associated clinical disease may be considered LGLT leukemia.4,5 As ever smaller clones are being detected with more sensitive technology, the distinction of these from LGLT leukemia is evolving.6

We performed sensitive flow cytometry to detect LGLT clones and correlated these with clinical disease. On the basis of this review, we propose three categories of LGLT clones: (1) T-cell clones of undetermined significance (TCUS), (2) LGLT leukemia, and (3) T-cell immunoclones (TICs).

Materials and Methods

From 2009 to 2013, flow cytometry for 24 variable regions of the T-cell receptor β chain (Vβ) was performed at the University of Minnesota on blood or marrow biopsy specimens that were submitted for routine patient care and that met the following criteria: absolute number of LGLTs in the blood exceeding 0.5 × 109/L, greater than 5% LGLTs in the blood leukocytes (if the WBC counts were not known), greater than 5% LGLTs in the marrow leukocytes, aberrant immunophenotypes on T cells (abnormal antigen expression by more than 1/3 to 1/2 log difference from normal relative to the closest normal population in
the same specimen), or high indexes of clinical suspicion for the possibility of clonal LGLT. Cases were excluded from analysis if there were known histories of prior transplants (bone marrow or solid organs) or of other neoplasms, unless there were high indexes of clinical suspicion for the possibility of concomitant LGLT clones. This study was approved by the institutional review board of the University of Minnesota and is in accord with the Helsinki Declaration of 1975.

The routine eight-color screening panel by flow cytometry (three-laser FACSCanto II; Becton Dickinson, Franklin Lakes, NJ) included CD2, CD3, CD4, CD5, CD7, CD8, CD45, and CD56 (Becton Dickinson; Beckman Coulter, Brea, CA) with fluorochromes fluorescein isothiocyanate (FITC), phycoerythrin (PE), peridinin chlorophyll protein–cyanin 5.5 (PerCP-Cy5.5), phycoerythrin–cyanin 7 (PE-Cy7), allophycocyanin (APC), allophycocyanin–cyanin 7 (APC-H7), V450, and V500. In most cases, this panel was expanded to include CD16 and CD57. The LGLT clones were quantitated as CD3-positive T cells expressing CD16, CD56, or CD57. The antibodies were added to whole blood or marrow after adjusting cellular concentrations, and the erythrocytes were lysed with ammonium chloride. The immunophenotypes of the LGLT clones were compared with that of normal T lymphocytes in the same specimen.

For cases fulfilling the selection criteria, additional analyses were performed for the T-cell receptors αβ and γδ and for Vβ. After lysing erythrocytes with ammonium chloride, Vβ analysis by flow cytometry was performed in four colors with CD3 and CD8 or in five or six colors if additional antibodies (CD4, CD5, CD56, etc) were needed to gate LGLT populations with aberrant immunophenotypes. The Vβ kit (IOTest Beta Mark; Beckman Coulter) has eight cocktails with 24 antibodies (Vβs 1, 2, 3, 4, 5.1, 5.2, 5.3, 7.1, 7.2, 8, 9, 11, 12, 13.1, 13.2, 13.6, 14, 16, 17, 18, 20, 21.3, 22, and 23) labeled with FITC, PE, or FITC and PE. Clonality was documented with the following criteria: a single Vβ expressed by more than 50% of a gated population or all 24 Vβs expressed by less than 30% of a gated population since the antibodies should stain 70% of T lymphocytes.

Vβ analysis was applied only to T cells expressing the αβ T-cell receptor.

Medical charts were reviewed for clinical findings present concurrently with the LGLT clones. These included the patient age, blood hemoglobin, WBC count, neutrophil count, platelet count, marrow cellularity, splenomegaly, transplants (bone marrow or solid organs), autoimmune disorders, and neoplasms. The medical charts were reviewed for treatment, survival, and cause of death.

**Results**

**Immunophenotype by Flow Cytometry**

Fifty-four (20%) of 264 patients with testing by Vβ had clonal abnormalities. The LGLT clones were CD4+/CD8+ in 67% (36/54), CD4+/CD8− in 9% (5/54), CD4+/CD8+ in 19% (10/54), and CD4−/CD8− in 6% (3/54). CD5− was positive in 96% (52/54). Coexpression of CD16 and CD57 was found in 32% (15/47), but 66% (31/47) lacked

**Table 1**

<table>
<thead>
<tr>
<th>Immunophenotype</th>
<th>Percentage of LGLT Clones, No./Total No. (%)</th>
<th>Aberrancies, No./Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4+/CD8−</td>
<td>5/54 (9)</td>
<td>2/54 (4), dim CD4</td>
</tr>
<tr>
<td>CD4+/CD8+</td>
<td>1054 (19)</td>
<td>10/54 (19), dim CD8</td>
</tr>
<tr>
<td>CD4−/CD8−</td>
<td>3/54 (6)</td>
<td></td>
</tr>
</tbody>
</table>

* Most expressed CD8 without CD4, but a minority coexpressed CD4 and CD8, albeit with aberrantly dim levels for one or the other.

**Table 2**

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Percentage of LGLT Clones Positive, No./Total No. (%)</th>
<th>Aberrancies, No./Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD2</td>
<td>54/54 (100)</td>
<td>8/54 (15), dim</td>
</tr>
<tr>
<td>CD3</td>
<td>54/54 (100)</td>
<td>6/54 (11), dim</td>
</tr>
<tr>
<td>CD5α</td>
<td>43/54 (80)</td>
<td>23/54 (43), dim</td>
</tr>
<tr>
<td>CD7</td>
<td>50/54 (93)</td>
<td>11/54 (20), negative</td>
</tr>
</tbody>
</table>

* CD5 was aberrantly dim or absent in most cases.

**Table 3**

<table>
<thead>
<tr>
<th>Abnormal Vβ</th>
<th>No./Total No. (%) of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vβ 2</td>
<td>2/54 (4)</td>
</tr>
<tr>
<td>Vβ 3</td>
<td>4/54 (7)</td>
</tr>
<tr>
<td>Vβ 5.1</td>
<td>1/54 (2)</td>
</tr>
<tr>
<td>Vβ 7.1</td>
<td>1/54 (2)</td>
</tr>
<tr>
<td>Vβ 8</td>
<td>4/54 (7)</td>
</tr>
<tr>
<td>Vβ 9</td>
<td>2/54 (4)</td>
</tr>
<tr>
<td>Vβ 13.1</td>
<td>4/54 (7)</td>
</tr>
<tr>
<td>Vβ 13.2</td>
<td>3/54 (6)</td>
</tr>
<tr>
<td>Vβ 14</td>
<td>5/54 (9)</td>
</tr>
<tr>
<td>Vβ 17</td>
<td>2/54 (4)</td>
</tr>
<tr>
<td>Vβ 20</td>
<td>2/54 (4)</td>
</tr>
<tr>
<td>Vβ 21.3</td>
<td>1/54 (2)</td>
</tr>
<tr>
<td>Vβ 22</td>
<td>2/54 (4)</td>
</tr>
<tr>
<td>Vβ 23</td>
<td>5/54 (9)</td>
</tr>
<tr>
<td>Lack all 24 Vβs</td>
<td>16/54 (30)</td>
</tr>
</tbody>
</table>

* Most cases had restriction for a single Vβ (38/54 [70%]).
The percentage of the LGLT clone in the marrow is shown as a percentage of LGLT cells in the aspirated marrow leukocytes (%MC) and as a percentage of marrow space (%MS). Although these percentages may not always be representative because of hemodilution, the %MS was calculated by multiplying the %MC by the percent marrow cellularity in the trephine biopsy. The %MS provided a better estimate of the clone size than did the %MC. For example, one patient with 33% MC had only 2.5% MS because the marrow had aplastic anemia. The %MC was less than 20% in 89% (31/35), less than 10% in 77% (27/35), and less than 5% in 60% (21/35) of cases. The %MS was less than 10% in 91% (31/34), less than 5% in 85% (29/34), and less than 2% in 59% (20/34).

The quantities of the clones in the blood and marrow were compared for those cases with concurrent specimens. Table 4. The ACC correlated better with the %MS than CD16, and one case expressed CD16 without CD57. CD56 was expressed at least partially in 94% (46/49).

After clonality was defined by Vβ, the clonal populations were backgated for comparison with the closest normal T lymphocytes (eg, CD8+ clones compared with normal CD8+ T cells in the same specimen), and it was found that, at times, there were clear differences from normal by more than 1/4 to 1/3 log immunofluorescence intensities that were not readily apparent before Vβ analysis and backgating. Aberrant immunophenotypes, including those identified by backgating, were found on 94% (51/54) of LGLT clones. Table 2. The most common immunophenotypic abnormality was decreased or absent CD5, which was found in 63% (33/54), although slightly decreased CD5 was occasionally seen in polyclonal LGLTs (data not shown).

All cases had clonal abnormalities for Vβ. Table 3. Restrictions for individual Vβs were found in 70% (38/54), although each Vβ was found in less than 10% of cases. Lack of all tested 24 Vβs was found in 30% (16/54); this is considered abnormal because these 24 Vβs should be expressed by 70% of T lymphocytes. All clones expressed the αβ T-cell receptor.

Size of the LGLT Clones

An absolute clone count (ACC) was calculated from the WBC count and from the percentage of clonal LGLTs in the blood Figure 1. The ACC provided a better estimate of the size of the clone than the percentage because many of these patients had neutropenia. For example, one patient with 67% clonal LGLTs had an ACC of only 0.6 × 10⁹/L because the WBC count was only 0.9 × 10⁹/L. ACC was less than 2.0 × 10⁹/L in 76% (19/25) and less than 0.5 × 10⁹/L in 60% (15/25).

Table 4. Comparison of the Size of the T-Cell Large Granular Lymphocyte Clone in the Blood and Marrow

<table>
<thead>
<tr>
<th>Case No.</th>
<th>ACC, ×10⁹/L</th>
<th>Clone %MC</th>
<th>Clone %MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.6</td>
<td>0.4</td>
<td>0.1</td>
</tr>
<tr>
<td>2</td>
<td>0.6</td>
<td>33</td>
<td>2.5</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>12</td>
<td>2.7</td>
</tr>
<tr>
<td>4</td>
<td>0.3</td>
<td>0.2</td>
<td>0.07</td>
</tr>
<tr>
<td>5</td>
<td>0.004</td>
<td>10</td>
<td>3.5</td>
</tr>
<tr>
<td>6</td>
<td>0.2</td>
<td>2</td>
<td>1.2</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>1.3</td>
<td>31</td>
<td>20</td>
</tr>
<tr>
<td>9</td>
<td>0.01</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>10</td>
<td>0.1</td>
<td>0.6</td>
<td>0.2</td>
</tr>
</tbody>
</table>

ACC, absolute clone count; %MC, marrow leukocytes; %MS, marrow space. *Low levels of ACC were associated with low levels of %MS.

The percentage of the LGLT clone in the marrow is shown as a percentage of LGLT cells in the aspirated marrow leukocytes (%MC) and as a percentage of marrow space (%MS) Figure 2, although these percentages may not always be representative because of hemodilution. The %MS was calculated by multiplying the %MC by the percent marrow cellularity in the trephine biopsy. The %MS provided a better estimate of the clone size than did the %MC. For example, one patient with 33% MC had only 2.5% MS because the marrow had aplastic anemia. The %MC was less than 20% in 89% (31/35), less than 10% in 77% (27/35), and less than 5% in 60% (21/35) of cases. The %MS was less than 10% in 91% (31/34), less than 5% in 85% (29/34), and less than 2% in 59% (20/34).

The quantities of the clones in the blood and marrow were compared for those cases with concurrent specimens Table 4. The ACC correlated better with the %MS than

© American Society for Clinical Pathology

Downloaded from https://academic.oup.com/ajcp/article-abstract/144/1/137/1762006 by guest on 01 May 2018

DOI: 10.1309/AJCPJ57YTEGLJU0I
Most cases with large clones in the blood or marrow also had large clones at the other site.

The ACC in the blood over time was generally stable, with limited follow-up, although there were exceptions, such as case 18, which had an increase from 6.9 to 40 × 10^9/L over 63 months. That patient had a history of rheumatoid arthritis and LGLT leukemia and was alive at last follow-up.

The quantity of the LGLT clone in the marrow over time was generally stable, with limited follow-up, although there were exceptions. The %MS was more stable than the %MC. For example, during treatment for aplastic anemia, patient 2 had a %MC decrease from 33% to 5%, while the %MS changed only slightly from 2.5% to 0.4%. Patient 4 had kidney and liver transplants and LGLT leukemia and was treated for that but died at least in part due to leukemia 7 years after the original diagnosis.

**Clinical Findings**

The patients’ ages ranged from 10 to 90 years, with a median of 68 years. Many of the patients were elderly. There were 50% males and 50% females. Anemia was found in 67% (16/24) of men, in 54% (13/24) of women, and in both children. Leukopenia and leukocytosis were found in 52% (26/50) and 16% (8/50), respectively. Neutropenia was present in 48% (24/50) and severe neutropenia (<0.5 × 10^9/L) in 20% (10/50). Most patients had thrombocytopenia (28/50 [56%])

Splenomegaly was detected in 14% (6/44) of patients. Four had large LGLT clones consistent with LGLT leukemia. A fifth had a myeloproliferative neoplasm, in addition to a 5% MS LGLT clone. A sixth patient with only slight splenomegaly had an ACC of 0.01 × 10^9/L, 0.2% MS, and neutropenia and was treated with granulocyte colony-stimulating factor, prednisone, and cyclosporin A.

Many of these patients with LGLT clones had concurrent clinical disease: eight (15%) had B-cell clones, including posttransplant lymphoproliferative disorder of diffuse large B-cell lymphoma (n = 1), hairy cell leukemia (n = 1), marginal zone B-cell lymphoma (n = 1), CD5+/
CD10− mature B-cell clones (n = 2), CD10+ B-cell clone (n = 1), or B-cell lymphomas (n = 2). Seven patients (13%) had myeloid neoplasms, including myelodysplastic syndromes (n = 5), myeloproliferative neoplasm (n = 1), or unclassified myeloid neoplasm (n = 1). Another patient had received recent chemotherapy for acute myeloid leukemia. Seven patients (13%) had myeloid neoplasms, including myelodysplastic syndromes (n = 5), myeloproliferative neoplasm (n = 1), or unclassified myeloid neoplasm (n = 1). Another patient had received recent chemotherapy for acute myeloid leukemia. Seven patients (13%) had myeloid neoplasms, including myelodysplastic syndromes (n = 5), myeloproliferative neoplasm (n = 1), or unclassified myeloid neoplasm (n = 1). Another patient had received recent chemotherapy for acute myeloid leukemia. Seven patients (13%) had myeloid neoplasms, including myelodysplastic syndromes (n = 5), myeloproliferative neoplasm (n = 1), or unclassified myeloid neoplasm (n = 1). Another patient had received recent chemotherapy for acute myeloid leukemia.

Ten (20%) of 51 patients had large LGLT clones: ACC greater than 2.0 × 10^9/L or %MS greater than 10%. An additional two patients had clinical histories of LGLT leukemias; at the time of this study, one had 4.5% MS and 10% MC, and the other had 6% MS and 9.5% MC. For the patient groups described here and below, the immunophenotypic differences between groups were for abnormalities in CD3 and for lack of Vβs, and these will be described for each group. Among this group of patients, one LGLT clone had bright CD3, and four LGLT clones lacked all of the tested Vβs. Five cases tested by polymerase chain reaction (PCR) for rearrangement of the T-cell receptor γ chain were monoclonal. Clinical follow-up was limited in this retrospective study, with only nine (18%) patients followed in the medical charts for more than 2 years, but three patients died at least in part due to LGLT leukemia at 7, 10, and 18 years after the original diagnosis; there was no splenomegaly or hepatomegaly at autopsy in one of those patients. A fourth patient with LGLT leukemia died, but the cause of death is unknown, and that patient had comorbidities, including renal failure and dementia.

Fifteen (29%) of 51 patients had small clones (ACC <2.0 × 10^9/L and %MS <10%) and associated findings limited to nonneoplastic disorders of the blood or marrow (excluding aplastic anemia) or hypothyroidism. None of these patients died of the LGLT clone, and most (n = 10) received no drug therapy for the LGLT clone or the cytopenias according to the available medical records; these patients’ ages ranged from 54 to 89 years. Most of these 10 patients had thrombocytopenia.
(4/7), anemia (6/7), neutropenia (3/7), or severe neutropenia (1/7). One LGLT clone had slightly dim CD3, and one LGLT clone lacked all of the tested Vβs. Two of these patients had more than one specimen tested over time, and those had stable levels of the LGLT clones over 7 to 25 months. One specimen tested by PCR for rearrangement of the T-cell receptor γ chain was monoclonal.

Four of the 15 patients were treated for cytopenias with growth factors or steroids, and one had Evan syndrome and received rituximab. A fifth patient with slight splenomegaly was treated as described above. For these five patients, most had thrombocytopenia (3/5), anemia (2/5), neutropenia (3/5), or severe neutropenia (1/5). Three patients had more than one specimen tested over time, and those showed stable levels of the LGLT clones over 3 to 45 months.

Twenty-six (51%) of 51 patients had an ACC less than 2.0 \times 10^9/L, %MS less than 10%, and no clinical histories of LGLT leukemias but had clinically significant associated diseases other than those described above, and those other disorders could account for cytopenias. The patient ages ranged from 10 to 84 years, and eight patients were younger than 54 years. For these patients, about one-third (n = 11) had abnormal expression of CD3, either dim or bright, and about one-third (n = 10) had LGLT clones lacking all tested 24 Vβs. Eight of these patients had more than one specimen tested over time, and those had stable levels of the LGLT clones over 3 to 69 months, with a rare exception described below. Three patients had PCR performed for the T-cell receptor γ chain, and two specimens were monoclonal; a third specimen from an aplastic marrow was oligoclonal. None of these patients had deaths that were attributed to the LGLT clone. The clinical management of these patients, however, was driven by treatment of the associated diseases, and some of those treatments could have effects on the LGLT clones, but it is not clear whether the clinical management of these patients was altered by knowledge of the presence of the small LGLT clones.

One patient, a 13-year-old girl, developed a posttransplant lymphoproliferative disorder of diffuse large B-cell lymphoma, as well as an LGLT clone with an ACC of 1.0 \times 10^9/L and 1% MS associated with an Epstein-Barr virus infection after bone marrow transplant for aplastic anemia. After treatment with rituximab, the size of the LGLT clone in the marrow decreased to 0.1% MS over 10 months.

Discussion

The 2008 WHO classification defines LGLT leukemia as a persistent increase in LGLTs greater than 2.0 \times 10^9/L in the blood without a known cause.1 The current study confirms that ACC is a better indicator of clone size than the percentage of circulating leukocytes because many of these patients have neutropenia.10 Similarly, the %MS is a better indicator of clone size than the %MC because many of these patients have hypocellular marrows, including aplastic anemia. In this study, large clones in the blood were generally associated with large clones in the marrow.

Once the clonality of LGLT is established, a 10-fold increase in the LGLT population would give an ACC greater than 2.0 \times 10^9/L or %MS greater than 10% (data not shown). If these criteria were used to define LGLT leukemia, 10 of the patients in this study would have leukemia, and an additional two patients had clinical histories of LGLT leukemias. Three of these patients had deaths due at least in part to the LGLT clone. Although splenomegaly is often associated with LGLT leukemias, it is interesting that one of the patients who died did not have splenomegaly or hepatomegaly at autopsy. The clinical course and treatment of LGLT leukemias have been reviewed elsewhere.8,11,12

About one-third of the patients had small LGLT clones and associated diseases limited to nonneoplastic disorders of the blood or marrow (excluding aplastic anemia) or hypothyroidism. Most of these patients were monitored but not treated for the LGLT clone, but a minority received growth factors or steroids for cytopenias.

About half of the patients had small LGLT clones and clinically significant associated diseases: B-cell clones, myeloid neoplasms, aplastic anemia, transplants, systemic autoimmune disorders, or carcinomas. In these patients, the associated disease and its treatment dominated the clinical course. It is not clear whether the presence of small LGLT clones influenced the clinical management since some of the treatment regimens would be similar to those recommended for LGLT clones. Clinical diseases associated with LGLT clones have been reviewed elsewhere.5,6,13-20

For patients with small LGLT clones, we propose the term T-cell clone of undetermined significance, which is slightly different from T-cell clonopathy of undetermined significance, as will be discussed below. The precise size of the clone to distinguish LGLT leukemia from TCUS is not well defined and will likely evolve over time, but we propose a 10-fold increase, which would be an ACC greater than 2.0 \times 10^9/L or %MS greater than 10% for the leukemia. If the marrow cellularity were not available to calculate the %MS, then greater than 20% of marrow cells in an aspirate would be suggested, although this percentage might not reflect the true extent of marrow involvement in patients with hypocellular marrows, such as aplastic anemia. Documentation of the persistence of the clone for 6 months would be recommended.

Similar terminology is used for other disorders, such as monoclonal gammopathy of undetermined significance. Monoclonal B-cell lymphocytosis is essentially a B-cell
clone of undetermined significance that is distinguished from chronic lymphocytic leukemia based on the size of the B-cell clone. The term leukemia is traditionally used for disorders with unregulated cellular proliferation as evidenced by large clones in the blood or marrow.

The term T-cell clonopathy of undetermined significance has been used in the medical literature for patients with varying sizes of LGLT clones to emphasize the indolent clinical course in many patients. Our proposed term would be restricted to those patients with small clones and omits the -opathy since some patients have no clinically significant disease, although the term T-cell clonopathy of undetermined significance has also been used for patients at the more benign end of the clinical spectrum.

These small LGLT clones had aberrant immunophenotypes and clonal abnormalities by Vβ. Most expressed CD8 without CD4, but a significant number coexpressed CD4 and CD8, as has been previously described. Small LGLT clones have also been reported previously. Most of these small LGLT clones did not change the clinical management, but there may be patients who need treatment for an LGLT clone because of its immunologic effects, such as cytopenias, even if the clone size were small. Although these small clones with associated immunologic disease may be referred to in the medical literature as LGTL “leukemias,” we propose that small clonal LGLTs associated with clinically significant immunologic effects be referred to as T-cell immunoclonal. The distinction between a TCUS and a TIC would be based on the clinical decision for a need to treat the immunologic effects of the LGLT clone, and then the term TIC could be applied rather than leukemia. The treatment would be because of the immunologic effects of the clone rather than its unregulated cellular proliferation. Similarly, the clinical need to treat autoimmune hemolytic anemia is not used to define the presence or absence of chronic lymphocytic leukemia in patients with monoclonal B-cell lymphocytosis. With extension of the terminology proposed here, monoclonal B-cell lymphocytosis would be a B-cell clone of undetermined significance, and if it were associated with an autoimmune hemolytic anemia that needed treatment, it would be considered a B-cell immunoclonal. This proposed terminology for LGLT clones would then be more consistent with the terminology used for other leukemias and would still accommodate the need for treatment of the immunologic effects of TICs even if the size of the clones was not sufficient to diagnose LGLT leukemia. To summarize, the proposed terminology for the clinical spectrum of LGLT clones is TCUS, LGLT leukemia, and TIC.

References


Corresponding author: Timothy P. Singleton, MD, HematoLogics, 3161 Elliott Ave. W, Suite 200, Seattle, WA 98121; tpsingleton@hematologics.com.

© American Society for Clinical Pathology


