A Case Report: Large Granular Cell Leukemia/Lymphoma (LGL)

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ABSTRACT

We presented a 64-year-old male patient with T-large granular cell leukemia/lymphoma with an aggressive clinical course. Large granular lymphocytes were noted on peripheral blood smear. The phenotyping of the cells was typical T-cell lineage [CD2 (+), CD3 (+), CD5 (+)]. Clonal rearrangement of the T-cell receptor gene (TCR) was demonstrated by DNA hybridization technique. Large granular cell leukemia/lymphoma is a distinct entity with specific clinicobiological aspects. The clinical spectrum is wide and immunophenotyping and genotyping studies need to make a diagnosis.

Key Words: Leukemia, Large granular.


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INTRODUCTION

The term of large granular cell lymphocytic leukemia (LGL) is based on the observation of clonality and demonstration of tissue invasion by the cells which have abundant cytoplasm containing azurophilic granules in bone marrow, liver and spleen. This disease may be classified into T- and NK-lineage. Typical T-cell lineage (CD3 (+), CD4 (-), CD8 (-), CD16 (-), CD56 (-) and TCRαβ (+) large granular lymphocytic proliferation of mature T-lymphocytes and natural killer (NK)-LGL characterized by CD3 (-), CD4 (-), CD8 (-), CD16 (-), CD56 (-) and TCRαβ (-) large granular cell proliferation of NK cell origin[1-5]. The diagnosis of LGL leukemia is suspected on the basis of a persistent express of large granular lymphocytes usually with neutropenia. Often these lymphoproliferative disorders are associated with autoimmune diseases such as rheumatoid arthritis, colitis ulcerosa[6,7]. Increased frequency of various lymphoproliferative malignancies occurring in organ allograft recipient’s patients has been documented[8]. These malignancies might have been associated with Epstein-Barr virus (EBV) infections and immunosuppressive treatments[9-11]. Although HTLV-I and II may be associated with some cases of LGL, data indicated that most patients are not infected with HTLV-I and II virus[12,13].

A CASE REPORT

A 64-year-old male patient was admitted to the Hematology and Oncology clinic with hepatosplenomegaly, scrotal and tibial oedema, pleural effusion and lymphadenopathies on the axillary, cervical and ingu-
inal regions. Leucocytosis, anemia and trombocytopenia was detected on his complete blood count (Table 1). Large granular lymphocytes were noted on peripheral blood smear (Figure 1). Bone marrow biopsy showed hypercellularity with leukemic blasts at a high percentage. Bilaterally pleural effusion, mediastinal, axillary multiple lymphadenopaties on thorax CT and splenomegal, paraaortic, paracaval and postpancreatic lymphadenopaties on abdominal CT were detected (Figures 2,3). Immunophenotyping showed that large granular lymphocytes were CD2 (+), CD3 (+), CD5 (+) and T-cell receptor gene rearrangement studies using DNA hybridization technique showed clonal rearrangement of T-cell receptor gene on his peripheral blood mononuclear cells. The biopsy of one of the largest cervical lymph nodes showed small lymphocytic lymphoma. Thoracic drainage for pleural effusion was performed for a few times. Treatment for large granular cell leukemia with chemotherapy including cyclophosphamide (750 mg/m², on day 1), doxorubicine (50 mg/m² on day 1), vincristine (1.4 mg/m² on day 1) and prednisolone (100 mg on days 1 through 5) was initiated. Chemotherapy cycles were repeated every 21 days (CHOP regimen). After three cycles, progression was detected and the patient died due to respiratory failure.

**DISCUSSION**

Large granular cell leukemia is diagnosed by increased numbers of lymphocytes and the presence of the cells that have abundant cytoplasm containing azurophilic granules but in some cases lymphocytes may appear normal and granules may be absent[14]. In our case, there were lymphocytes that have large granules and abundant cytoplasm in the peripheral blood and bone marrow. The characteristic phenotype of T-LGL was also seen on the lymphocytes and it was found that these malignant cells expressed CD2, CD3, CD5 by flow cytometry. Additionally, the patient had monoclonal T-cell gene rearrangement as a support for the diagnosis of T-LGL. The mechanism of persistent lymphocytosis in large granular cell leukemia may be in defects in CD3 activation or Fas crosslinking-induced cell death. It has been shown that inhibition of me-

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### Table 1. Hematological features

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<td>44</td>
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<td>Hb</td>
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**Figure 1.** The appearance of peripheral blood smear.

**Figure 2.** Bilateral pleural effusion, consolidation, multiple mediastinal and axillary lymphadenopathies on CT scan.

**Figure 3.** Splenomegal, paraaortic, paracaval and postpancreatic lymphadenopathies on abdominal CT scan.
The immunophenotyping of T-LGL is CD3 (+), CD4 (-), CD8 (+), CD16 (+), CD56 (-), CD57 (+). NK-LGL cells are usually CD3 (-), CD4 (-), CD8 (-), CD16 (+), CD56 (+) and CD57 (-). Although NK-LGL has an acute fulminant course with hepatosplenomegaly, fever and pancytopenia, chronic form of disease can occur with a clinical course similar to that of T-LGL[24].

In this report, we presented a case of T-LGL with an aggressive clinical course.

**REFERENCES**


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