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# A rare case report of Chronic Lymphocytic Leukemia: Transformation and Progression of Chronic Lymphocytic Leukemia to Prolymphocytic Leukemia

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## ABSTRACT

**Background:** Chronic lymphocytic leukemia, or CLL, is a chronic hematological malignancy marked by the overproduction of mature but nonfunctional lymphocytes. This condition is uncommon among Asian individuals. As a result, variations of this type of CLL are even less frequently observed. A CLL that presents with prolymphocytic progression is now recognized as a new illness in the fifth edition of the World Health Organization classification. It is identified as a CD5+ non-mantle B-cell tumor featuring a minimum of 15% prolymphocytes in the bloodstream or bone marrow, and it partially supersedes the previous classification of B-cell prolymphocytic leukemia. **Case Presentation:** A 78-year-old woman experiencing increasing fatigue and difficulty breathing was brought to the emergency room and subsequently found to have Chronic lymphocytic leukemia. In this report, we highlight an uncommon instance of prolymphocytic leukemia advancement in a CLL patient within an exceptionally brief period of one week. **Conclusion:** Prolymphocytic transformation of CLL is a rare case with poor prognosis. This change was illustrated by the presence of undeveloped cells found in the peripheral blood, resembling prolymphocytes. The CLL patient unfortunately passed away shortly after being admitted to the hospital for a few days, which is atypical for traditional CLL patients who generally experience a longer duration of life. Thus, it is necessary to monitor the number of prolymphocyte in CLL patient as indicator of poorer transformation of chronic leukemia.

**Keywords:** Chronic lymphocytic leukemia, Progression, Prolymphocytic Leukemia, Transformation

## INTRODUCTION

Chronic lymphocytic leukemia (CLL) is a hematological malignancy that is caused by the chronic proliferation of B-cells in a lymphoproliferative manner.<sup>1</sup> The blood and lymphatic system is affected by chronic lymphocytic leukemia, which is a disease where mature B-cells with CD5 positivity clonally proliferate and accumulate.<sup>2</sup> This illness is the most prevalent type of leukemia in Western countries. The median age for patients diagnosed with CLL is 70 years old.<sup>3,4</sup> In order to make a diagnosis, tests involving blood counts, blood smears, and the identification of circulating B-lymphocytes through immunophenotyping are conducted. This process aims to detect a clonal population of B-cells characterized by the presence of the CD5 antigen along with standard B-cell markers.<sup>2</sup>

Individuals diagnosed with CLL can progress to B-cell prolymphocytic leukemia. This condition is characterized by two different types of cell groups where prolymphocytes make up more than 15%, alongside the small round lymphocytes typical of CLL. This clinical evolution was linked to a transformation in cell structure, transitioning from minor lymphocytes to an expanding group of significantly changed lymphocytes found in the bloodstream, bone marrow, and lymphatic glands. At the time of transformation, the spleen generally appears larger than it does at the point when CLL is diagnosed. Transformation is believed to be linked to a greater resistance to treatment and reduced life expectancy, even though the majority of fatalities

took place in clinical Stages III and IV, which are recognized for their unfavorable outlook.<sup>4,5</sup>

Individuals are at a higher risk for autoimmune hemolytic anemia (indicated by a positive Coombs test) as well as autoimmune thrombocytopenia. These B cells ultimately disseminate across the entire body, leading to widespread symptoms including elevated temperature, nocturnal perspiration, unintended loss of weight, tiredness, and feeling full quickly. The lack of functioning B cells reduces the ability of the body to produce antibodies essential for immune responses, resulting in hypogammaglobulinemia, which ultimately heightens the likelihood of infections.<sup>6</sup>

## CASE

A 78-year-old woman arrived at the emergency room experiencing increased fatigue and difficulty breathing. Physical examination showed splenomegaly without lymphadenopathy. Laboratory examination results showed thrombocytopenia (thrombocytes:  $12 \times 10^3/\mu\text{L}$ ), anemia (hemoglobin: 3.2 g/dl), and hyperleukocytosis (white blood cell count:  $176 \times 10^9/\text{L}$ ), lymphocyte predominance (90%) and neutropenia (polymorphonuclear neutrophils 5%), elevated creatinine 2.1 mg/dL, elevated uric acid 11.2 mg/dL (Figure 1, Table 1).

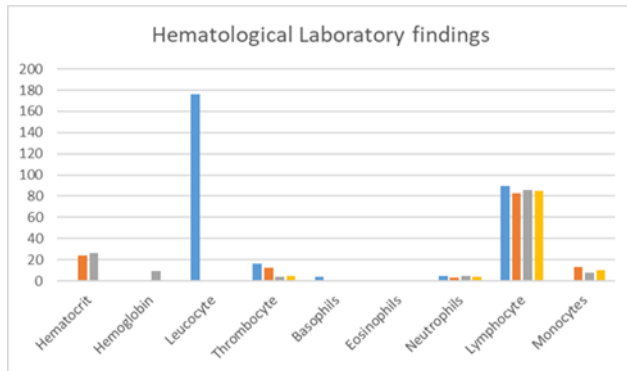
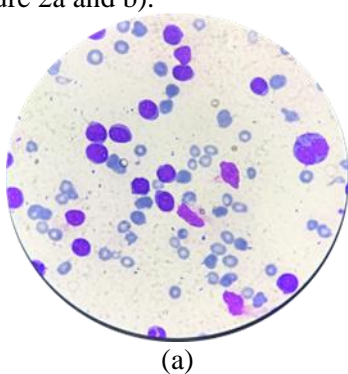


Figure 1. Routine blood laboratory tests during treatment

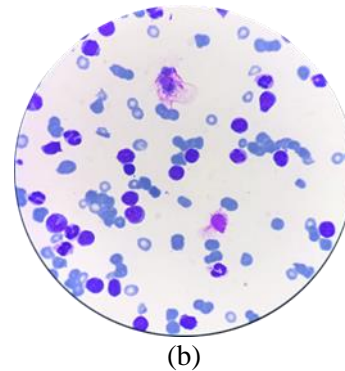
Table 1. Metabolic Panel

Laboratory test	Result	Reference range
Sodium	120	131-145 mmol/L
Potassium	5.7	3.5-5.1 mmol/L
Chlorida	95	97-107 mmol/L
Ureum	76	7-30 mg/dL
Creatinine	2.1	0.70-1.30 mg/dL
Uric acid	11.2	3.5-7.2 mg/dL
Albumin	3.2	3.5 to 5.5 g/dL

Peripheral blood smear showed significantly increasing cell number of leukocytes with lymphoid lineage predominance which have characteristics of small-medium size, basophilic scanty cytoplasm, round shaped nuclei, a single central nucleus, some are eccentric, grooved, mostly prominent single (medallion) nucleoli, some with multiple nucleoli. Smudge cells were easily seen in peripheral blood smear (Figure 2a and b).



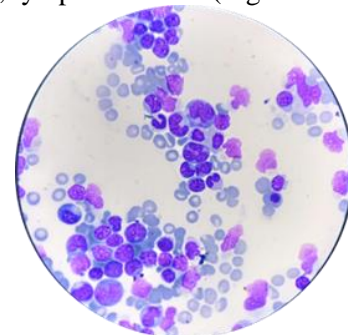
(a)



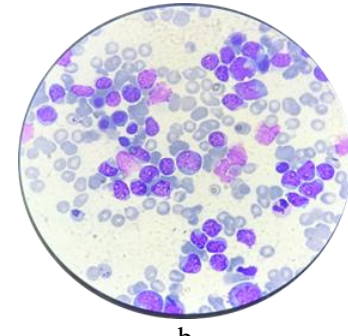
(b)

Figure 2 (a and b). Peripheral blood smear showed significantly increasing cell number of leukocytes with lymphoid lineage predominance (mature like lymphocyte 90%).

Bone marrow aspiration showed decreased thrombopoiesis, granulopoiesis, and erythropoiesis. However, lymphopoiesis elevated. Differential count in bone marrow aspiration predominated by mature like lymphocytes 55%, prolymphocytes 24%, lymphoma 5%, lymphoblast 1% (Figure 3a and b).



a



b

Figure 3 (a and b). Bone marrow aspiration showed decreased thrombopoiesis, granulopoiesis, and erythropoiesis, predominated by lymphoid lineage cells; mature like lymphocytes 55%, prolymphocytes 24%, lymphoma 5% and lymphoblast 1%

We performed flowcytometry analysis to confirm the lineage of predominance cells. The result [Figure 4] showed that the cell population in the CD45dim area predominantly expresses CD34+ which expressed T-cell associated antigens (CD7 and CD3).

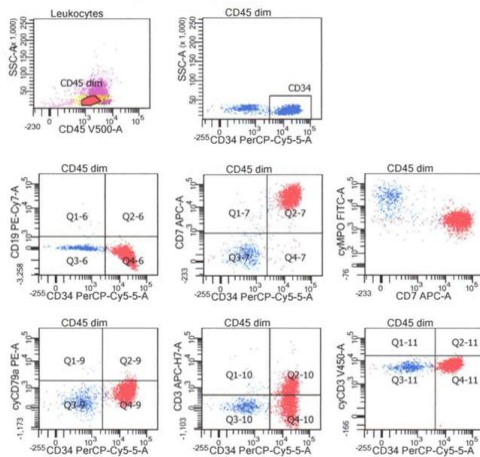


Figure 4. Flow cytometry analysis performed on blood revealed a blast population (blue) CD45dim expressed CD34+ which expressed T-cell associated CD7 and CD3.

## DISCUSSION

Chronic lymphocytic leukemia, or CLL, is identified as a type of lymphoproliferative disorder that involves the growth and gathering of mature lymphocytes that appear normal in structure but lack proper immune function. Smudge cells that are readily identifiable in the peripheral blood smear back up the theory of chronic lymphocytic leukemia. The main areas affected by the disease encompass the liver, spleen, lymphatic nodes, and bone marrow. However, in this case no lymphadenopathy found in patient.<sup>1,2</sup>

Bone marrow aspiration showed the elevation of mature like (small round) lymphocyte (55%) accompanied with prolymphocyte (24%) indicating CLL with prolymphocytic progression. This prolymphocytic progression variant was a rare case of CLL which associated with poor prognosis due to poor therapy response and shorter survival. This CLL case might be a transformation to prolymphocytic leukemia.<sup>3,7,8,9,10</sup>

The shape and form of cells during the prolymphocytic phase of CLL display a range of cell types at different levels of change. The identified cell types included small lymphocytes, large reactive lymphocytes, prolymphocytes, and infrequently seen blast-like cells. Transformation is characterized by having over 15% prolymphocytes, as indicated by the WHO.<sup>4</sup>

Neoplastic lymphoid cell invasion in the spleen and marrow brings about splenomegaly and a densely populated bone marrow. This enlargement of the spleen results in heightened retention of red blood cells and platelets, resulting in anemia and a drop in platelet count. Subsequently, patients demonstrate a

greater vulnerability to autoimmune hemolytic anemia and autoimmune thrombocytopenia. This patient exhibited symptoms of anemia such as exhaustion and difficulty breathing.<sup>4,5</sup>

Immunophenotyping rarely used for the diagnosis of chronic hematology malignancy. However, it plays major role in the diagnosis of this CLL variant. Flowcytometry showed CD3 and CD7 indicating the cell predominance of this patient is T-lineage of lymphoid. Usually, CLL does not show the presence of CD34 due to the absence of blast cells. The less mature type of lymphoid lineage also usually does not show the signal of CD34. However, CD34 was expressed from faint signal of CD45dim. This finding showed that the patient had cells in the middle stage between immature blast and mature lymphoid cells. It suggests there was transformation occur in the disease development. This idea is supported with the finding of prolymphocyte number more than 15% indicating the prolymphocytic progression of CLL, a transformation to prolymphocyte leukemia. This progression had been associated with poor prognosis. The patient of this case report died soon after hospitalized for several days. Thus, it is necessary to monitor the number of prolymphocyte in CLL patient as indicator of poorer transformation.<sup>5,6,10</sup>

## CONCLUSION

Prolymphocytic transformation of CLL is a rare case with poor prognosis. This change was linked to the emergence of a group of cells in the peripheral blood that looked like immature prolymphocytes. The main distinguishing morphological trait was the identification of two separate cell groups: the usual CLL lymphocytes and the prolymphocyte cells. This transformation can be recognized through both morphological characteristics and surface marker specifications. Prolymphocyte should be considered to be monitored as indicator of poorer transformation of CLL

## Ethical Approval

There is no ethical approval.

## Acknowledgments

The authors affirm that we have neither financial affiliation (e.g., employment relations, ownership of resources, grants, expert consultation, or patent registration) nor involvement with commercial organisations with direct financial interests in the subject or materials discussed in this manuscript nor such arrangements. Any other potential conflict of interest is disclosed.