Clin. Lab. 2025;71:XXX-XXX

CASE REPORT

Conversion of Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma to Angioimmunoblastic T-cell Lymphoma: a Rare Case

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SUMMARY

Background: **Angioimmunoblastic T-cell lymphoma (AITL) is a distinct subtype of peripheral T-cell lymphoma (PTCL) and accounts for 2% of all non-Hodgkin lymphomas. Its typical characteristics include an aggressive course, progressive lymphadenopathy, hepatosplenomegaly, systemic symptoms, anemia, hypergammaglobulinemia, and generally poor prognosis.**
Methods: **We describe a rare case in which the left inguinal lymph node was completely excised and biopsied one year ago. Based on histomorphology and immunohistochemistry, B-cell small lymphocytic lymphoma (CLL/SLL) was diagnosed. Routine bone marrow examination indicated the presence of immature lymphocytes; however, immunophenotyping showed no significant abnormal lymphocytes. One month ago, the patient developed swelling in the left lower limb, which gradually worsened. A fine-needle aspiration biopsy of the left inguinal lymph node revealed angioimmunoblastic T-cell lymphoma.**
Results: **The final diagnosis for this patient is a transformation from B-cell small lymphocytic lymphoma to angioimmunoblastic T-cell lymphoma (AITL) one year after the initial diagnosis.**
Conclusions: **In this report, we present a rare case of AITL. The aim is to enhance awareness among readers regarding the clinical, immunological, and phenotypic characteristics of various forms of AITL.**
(Clin. Lab. 2025;71:xx-xx. DOI: 10.7754/Clin.Lab.2024.240743)

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Case Report accepted August 1, 2024

KEYWORDS

B-cell small lymphocytic lymphoma, angioimmunoblastic T-cell lymphoma, rare

INTRODUCTION

Angioimmunoblastic T-cell lymphoma (AITL) is a rare subtype of peripheral T-cell lymphoma (PTCL) that originates from follicular helper T-cells (TFH) and is characterized by an infiltration of atypical medium-sized lymphocytes [1]. Its incidence is low, accounting for only 1% to 2% of all non-Hodgkin lymphomas [2]. The median age of onset for AITL is 65 years, and it is frequently associated with Epstein-Barr virus (EBV) infection. Over 80% of patients present at an advanced stage (Ann Arbor stage III - IV) at the time of diagnosis, leading to an overall poor prognosis [3]. Observing a transformation from B-cell small lymphocytic lymphoma (CLL/SLL) to AITL is exceedingly rare in clinical

practice. Here, we present a case of such a transformation occurring one year after the initial diagnosis of small B-cell lymphoma, with the aim of enhancing the understanding of this disease.

CASE REPORT

The patient, a 72-year-old male, presented with left-sided inguinal lymphadenopathy of unknown origin over a year ago. Pathological examination revealed structural destruction of the right inguinal lymph node with diffuse and nodular proliferation of small B lymphocytes. This led to a diagnosis of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) based on immunohistochemical staining. Immunohistochemistry results were as follows: CD10(+), BCL-6(+), CD30(-), CD3(-), CD21(FDC+), CK-P(-), BCL-2(-), CD23(+), CD43(-), CD5(+), Cyclin D1(-), CD20(L26)(+), Ki-67 (+30%) (Figure 1A). Bone marrow examination showed the presence of immature lymphocytes. Immunophenotyping did not reveal significant abnormal lymphocytes. Observation without treatment was recommended.

Two months ago, the patient noticed an enlargement of the left inguinal lymph node but did not seek medical attention. One month ago, he experienced progressive swelling of the left lower limb without fever, chills, chest tightness, shortness of breath, cough, sputum, abdominal pain, distension, headache, or dizziness. Physical examination revealed scattered pruritic skin rashes and multiple enlarged lymph nodes in the cervical, axillary, and inguinal regions. The largest lymph node, located in the left inguinal area, measured approximately 5 x 3 cm, was firm, poorly mobile, and non-tender. Swelling of the left lower limb was also observed.

Upon admission, laboratory results were as follows: blood β2-microglobulin 4.80 mg/L; C-reactive protein 9.38 mg/L; hemoglobin 114 g/L; platelet count 189 x 10^9/L; gamma-glutamyl transferase 85 U/L; potassium 2.83 mmol/L; lactate dehydrogenase 288 U/L; serum immunoglobulin IgM 412.00 mg/L; ferritin 361.03 ng/mL; EBV-DNA 4.74 x 10^3 copies/mL; cytomegalovirus DNA below detection limit; hepatitis B virus DNA quantification below detection limit.

Under ultrasound guidance, a fine-needle aspiration biopsy of the left inguinal lymph node was performed. The pathological findings of the lymph node biopsy were as follows: CD3(+), CD20(-), Ki-67(+, 40%), Bcl-2(+, 50%), Bcl-6(+), CD5(+), CD10(+), CD23(+, FDC), Cyclin D1(-), CD21(+, FDC), CD30(-), SOX11(-), EBER(+, scattered), CK(pan)(-), CXCL13(+), PD-1(+) (Figure 1B). The pathological diagnosis indicated angioimmunoblastic T-cell lymphoma (AITL). Bone marrow flow cytometry showed an abnormal T-lymphocyte population constituting approximately 1.44% of non-erythroid cells, expressing CD2, CD7, CD5, CD4, and CD45RO, but not expressing CD3, CD8, CD56, CD25 or CD45RA. Bone marrow cytology revealed atypical lymphocytes (Figure 1C - D).

Based on relevant auxiliary examinations, the final diagnosis for this patient is a transformation from small B-cell lymphoma to angioimmunoblastic T-cell lymphoma (AITL) one year after the initial diagnosis. Considering the patient's underlying condition of hypertension, treatment during hospitalization included diuretics such as furosemide and spironolactone to reduce edema, loratadine tablets for allergies, levofloxacin injections for infection, and supplementation with potassium and calcium. The patient's left lower limb swelling showed slight improvement, and the generalized rash significantly subsided. Considering the patient's financial situation and the family's wishes, further treatment was ultimately declined, and the patient was discharged.

DISCUSSION

This case illustrates a rare instance of transformation from small B-cell lymphoma to angioimmunoblastic T-cell lymphoma (AITL) one year post initial diagnosis. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is the most prevalent adult leukemia. It has been reported that a subset of patients with CLL/SLL may experience a transformation into an aggressive disease [4]. Furthermore, several epidemiological studies have indicated that patients with CLL/SLL are at an elevated risk of developing secondary cancers, including other hematologic malignancies. The occurrence of cutaneous or systemic T-cell tumors in patients with CLL/SLL has been documented extensively in case reports and series [5,6]. Mechanistically, the development of lymphomas is associated with the accumulation of oligoclonal or monoclonal T-cell populations exhibiting abnormal phenotypes or functional disruptions commonly observed in patients with CLL/SLL. It is well known that AITL exhibits varying degrees of EBV-positive or EBV-negative B-cell or plasma cell proliferation, usually polyclonal and sometimes monoclonal. Typically, this B-cell population consists of a small number of EBV-positive large B-cells, which occasionally progress to EBV-positive diffuse large B-cell lymphoma. The progression of small B-cell lymphoma to a T-cell lineage lymphoma is exceedingly rare.

A large epidemiological study has indicated that men with chronic lymphocytic leukemia (CLL) have an elevated risk of developing cutaneous T-cell lymphoma compared to the general population [7]. In CLL, the occurrence of T-cell lymphoma is associated with disruptions in T-cell homeostasis and immune regulation. CLL is linked to alterations in the immune system and immunodeficiency, as well as both quantitative and qualitative disturbances in the T-cell compartment of the blood. Clinically, this manifests as decreased immune surveillance and increased susceptibility to infections [8]. The complex interactions between CLL cells and T-cells result in chronic T-cell stimulation, leading to an increase in CD4+ and CD8+ T-cell subsets in the blood and the accumulation of abnormal oligoclonal/

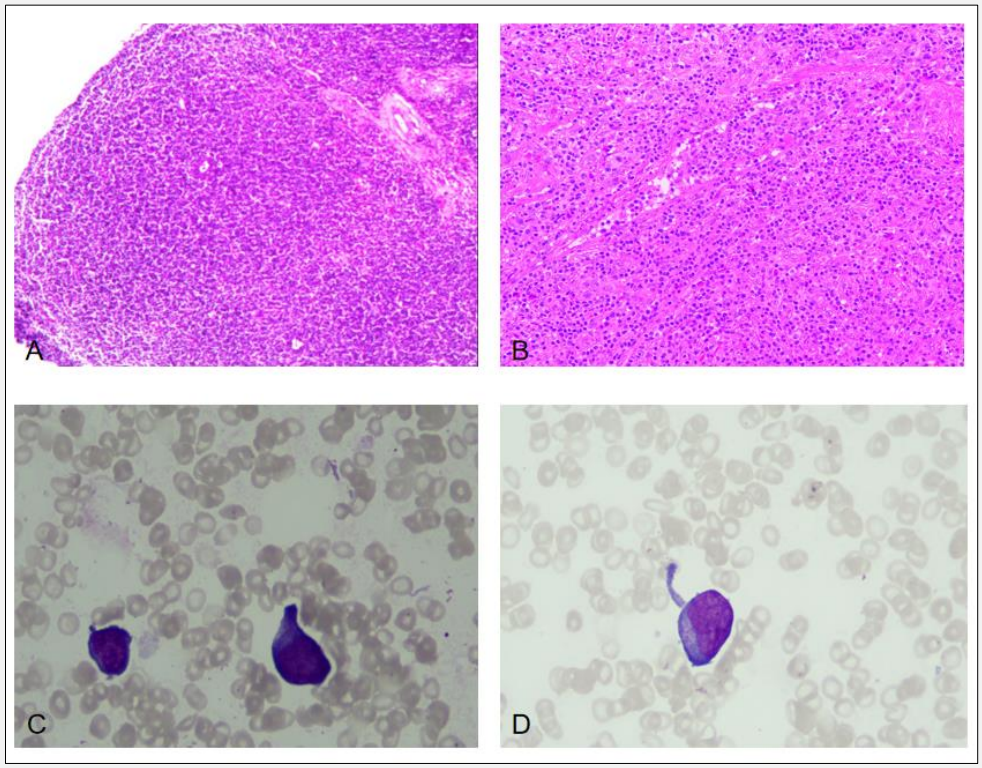

Figure 1. (A) The first biopsy of the right inguinal lymph node diagnosed B small lymphocytic lymphoma (CLL/SLL). (B) On the left side of the second inguinal lymph node biopsy diagnosis of vascular immune t-cell lymphoma. (C - D) Second bone marrow cytology revealed atypical lymphocytes.

monoclonal T-cell populations [9]. Different types of CD4+ helper T-cells show increased frequencies in CLL patients, expressing exhaustion markers such as PD1, CD60, and CD61 [10]. Notably, the frequency of TFH cells in the blood is notably higher in CLL/SLL patients. Therefore, it is speculated that these abnormal CD4+ T-cell populations may represent the progenitor cells of CD4+ T-cell lymphomas, particularly AITL. To date, there have been no reported cases of untreated small B-cell lymphoma transforming into AITL. The patient described in this report underwent a transformation from small B-cell lymphoma to AITL one year post-initial diagnosis. In summary, the transformation of small B-cell lymphoma to AITL one year after post-diagnosis is clinically rare and warrants aggressive treatment. Such patients typically have a poor prognosis, and the specific mechanisms underlying this transformation necessitate further investigation.

Declaration of Interest:
All authors declare no competing interests.

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