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Case study

TCL-1–positive hematogones in a patient with T-cell prolymphocytic leukemia after therapy☆

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Summary T-prolymphocytic leukemia (T-PLL) is a rare mature T-cell neoplasm characterized by proliferation of prolymphocytes. Most cases involve the T-cell leukemia-1 (*TCL1*) gene at 14q11.2 resulting in overexpression of TCL-1, which is helpful for distinguishing T-PLL from other T-cell neoplasms. We report a patient with T-PLL whose leukemic cells were positive for TCL-1 by immunohistochemistry but with a normal karyotype. The patient had anti-CD52 antibody therapy for 12 weeks. In a follow-up bone marrow biopsy specimen, numerous TCL-1–positive cells were present, which raised the differential diagnosis of residual T-PLL. However, further immunophenotypic studies confirmed that these cells were hematogones. Therefore a diagnosis of recovering bone marrow was established. The patient underwent stem cell transplant and is now in complete remission. This case demonstrates that hematogones can express TCL-1, and this knowledge is very important for the differential diagnosis in the follow-up marrow of T-PLL patients.

1. Introduction

T-cell prolymphocytic leukemia (T-PLL) is a rare mature T-cell leukemia characterized by a rapidly rising leukocyte count and proliferation of prolymphocytes, usually with a T-helper cell immunophenotype [1,2]. Most patients present with marked lymphocytosis (lymphocyte count often $\geq 100 \times 10^9$/L), and leukemic cells are found in the peripheral blood, bone marrow (BM), lymph nodes, spleen and sometimes skin. Patients with T-PLL often have an aggressive clinical course with a median overall survival of less than one year [3-7]. However, it is also recognized that a subset of T-PLL patients presents initially with an indolent clinical course, which becomes aggressive later in the course of disease [8,9].

Most T-PLL cases are associated with inv(14)(q11;q32) or t(14;14)(q11;q32). These chromosomal abnormalities juxtapose T-cell leukemia-1 (*TCL1*) next to a T-cell receptor (*TCR*) locus, resulting in overexpression of TCL-1 oncoproteins [10,11]. Currently TCL-1 is a useful marker for the diagnosis and differential diagnosis of T-PLL as it is not expressed in other mature T-cell lymphomas. It is also useful for detecting residual T-PLL in follow-up marrow biopsies.

In this report, we describe a patient with T-PLL who was treated with anti-CD52 antibody (Campath) therapy. A follow-up BM biopsy after therapy showed numerous TCL-1–positive cells in the biopsy specimen, but no evidence of an aberrant T-cell immunophenotype by flow cytometry. Further studies identified the TCL-1–positive cells to be B-cell precursors, that is, hematogones. This case is instructive in that realizing hematogones can be TCL-1 positive will help others avoid a potential misdiagnosis of residual disease in this context.

☆ Competing interests: The authors declare no competing interests.

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2. Case report

A 64-year-old African American man with a history of autoimmune thyroiditis presented with skin lesions and diffuse lymphadenopathy. A complete blood count showed marked leukocytosis with lymphocytosis (WBC: 25.1 × 10^9/L with 80% lymphocytes and 16% neutrophils). The peripheral blood smear showed many small- to intermediate-sized cells with a single distinct nucleolus, scant basophilic cytoplasm and cytoplasmic protrusions in occasional cells (Fig. 1A). Bone marrow aspiration and biopsy showed leukemic cells represented 25% of marrow cellularity (Fig. 1B). Immunohistochemical stains on the BM biopsy specimen showed that the neoplastic cells were positive for TCL-1 (Fig. 1C). Flow cytometric immunophenotyping analysis performed on the bone marrow aspirate showed aberrant T-PLL cells (approximately 70% of total events, 99.7% of total lymphocytes) with bright expression of CD2, CD3, CD4, CD5, CD7, CD25 (partial), CD26, CD52, and T cell receptor (TCR) α/β; and negative for CD1a, CD8, CD10, CD16, CD19, CD30, CD33, CD34, CD38, CD56, CD57, CD117, HLA-DR, MPO, TCR, and TdT (Fig. 1D). TCR V-β analysis showed monoclonal VB2 (Fig. 1D). Monoclonal T-cell receptor β and γ chain gene rearrangements were detected by polymerase chain reaction analysis. The diagnosis of T-PLL was established; however, conventional cytogenetic analysis showed a diploid male karyotype, 46,XY[20] on the 24-hour and 72-hour cultures of bone marrow specimen using phytohemagglutin to induce mitosis.

Since the initial bone marrow diagnosis of T-PLL, the patient has received Campath therapy for 12 weeks. After Campath treatment, his peripheral blood showed significant improvement in leukocytosis and lymphocytosis: WBC: 2.4 × 10^9/L; 73.3% neutrophils and 11% lymphocytes. Subsequently he underwent follow-up BM examination. BM aspirate smears showed 19% lymphoid cells with round regular nuclear contours, homogeneous chromatin, invisible nucleoli, and scant cytoplasm (Fig. 2A). The BM core biopsy specimen showed a mild lymphoid infiltrate composed of small- to intermediate-sized cells (Fig. 2B). Immunohistochemical analysis showed that the cells were positive for TCL-1 (Fig. 2C), which initially raised the possibility of residual T-PLL. However, flow cytometry analysis identified no aberrant T cells.

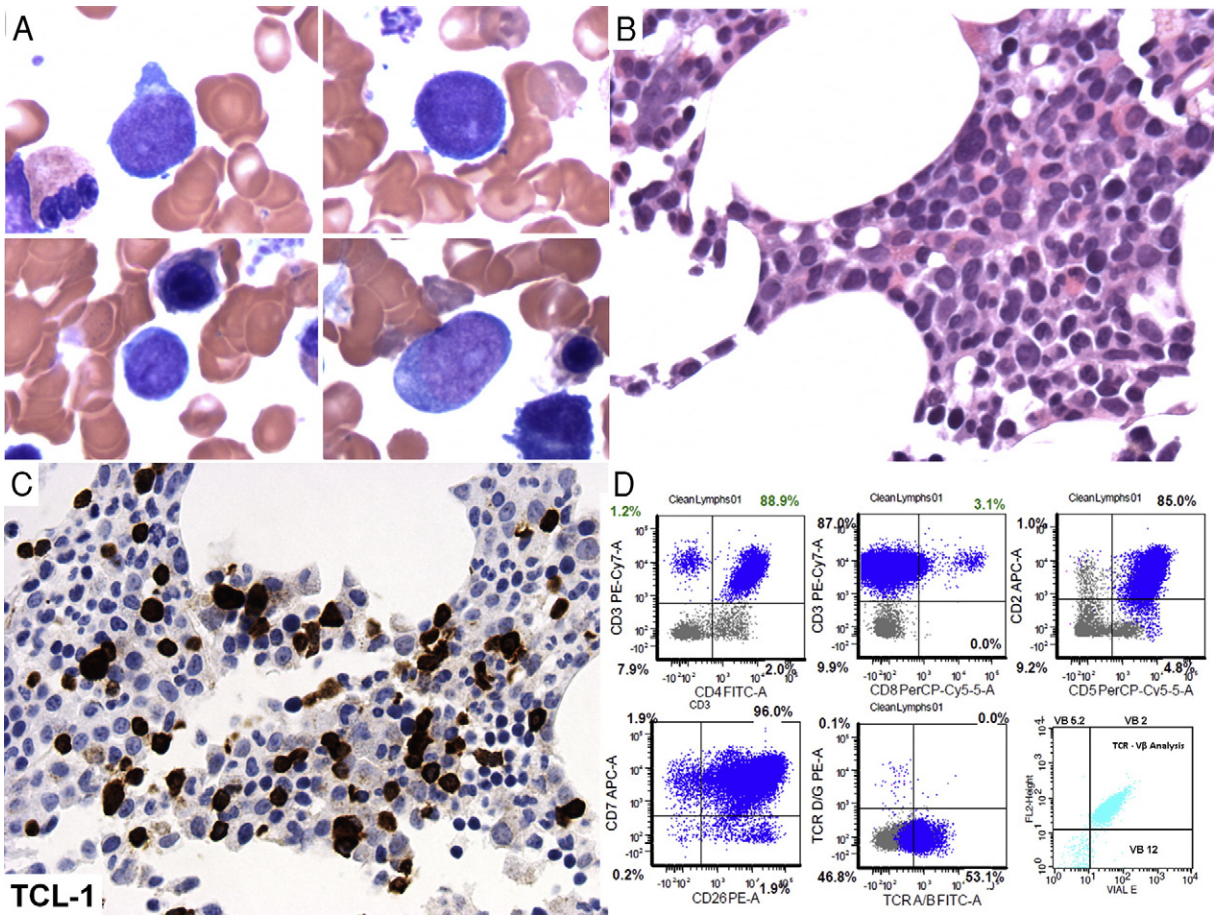

Fig. 1 Histopathologic and immunohistochemical findings of T-PLL. A, Peripheral blood smear shows lymphocytosis with numerous characteristic T-PLL prolymphocytes (Wright-Giemsa; ×1000). B, Bone marrow biopsy shows a variable cellular marrow with interstitial lymphoid infiltrate (hematoxylin and eosin, H&E; ×400). C, TCL-1 immunohistochemical stain highlights interstitial T-PLL cells (×400). D, Flow cytometry analysis of bone marrow aspirate reveals a clonal T cell population (TCR V-β analysis, lower right corner).