A 75-year-old man was referred to us with an outside diagnosis of T-cell prolymphocytic leukemia (T-PLL) posttreatment. He had mild leukocytosis (white blood cell count, $11.5 \times 10^9$/L) and multicompartmental lymphadenopathy by positron emission tomography–computed tomography (panel A) (maximum standardized uptake value, 6.3). A bone marrow (BM) biopsy showed no lymphoid infiltrate, and results of concurrent flow cytometry immunophenotyping (FCI) were negative. An axillary lymph node (LN) biopsy was subsequently performed. FCI failed to reveal aberrant T cells within lymphocyte gate but showed a large CD45 $^+$ population (CD2$^+$CD5$^+$CD4$^+$CD8$^+$CD7$^{bright}$ $+$ CD26$^{bright}$ $+$ CD52$^-$) negative for surface CD3 (sCD3) and CD45 (panels B–D; FITC, fluorescein isothiocyanate; PE, phycoerythrin; SSC, side scatter). Hematoxylin and eosin (panel E; original magnification $\times 40$) and immunohistochemical stains of LN biopsy showed architectural effacement by small to medium-sized neoplastic T cells that were cytoplasmic CD3$^+$CD4$^+$CD8$^+$TCL1$^+$ (panels F–G, original magnification $\times 40$) and negative for CD34/CD45/CD1a or terminal deoxynucleotidyltransferase (panel H, original magnification $\times 40$). Fluorescence in situ hybridization (FISH) using a TCL-1 break-apart probe was positive for TCL-1 rearrangement (panel I). BM FCI was retrospectively reanalyzed to include CD45$^-$sCD3$^-$ cells and revealed minimal involvement by T-PLL (0.3%) (panels J–K).

T-PLL is a rare, aggressive, mostly CD45$^+$sCD3$^+$ postthymic T-cell leukemia. In 5% to 10% of cases, either of these markers may be negative; however, simultaneous loss of both is extremely rare. This is problematic, since most of the FCI assays for T-cell lymphoma/leukemia focus on lymphocytes as defined by CD45/side scatter, with additional analysis on CD3$^+$ cells. This is challenging when the initial immunophenotype is unknown and involvement is minimal. Understanding this immunophenotype and using alternative gating strategy are essential to avoid false-negative results.