Data S1. Supplementary methods.

Flow cytometry protocol and antibody panels. Peripheral blood flow cytometry was performed using EDTA-anticoagulated peripheral blood. The assay was performed using fluorochrome-conjugated monoclonal antibodies to evaluate cellular antigen expression, together with forward- and side-scatter characteristics to assess cell size and intracellular granularity. Briefly, erythrocytes were lysed, and nucleated cells were washed and stained with monoclonal antibody panels according to routine clinical laboratory procedures. The monoclonal antibodies and associated reagents were mainly supplied by BD Biosciences. Data were acquired using a BD FACSCanto or BD FACSLyric flow cytometer and analyzed using BD FACSDiva software version 8.0.2 (all BD Biosciences). In each antibody-fluorochrome combination listed below, the antibody and fluorochrome served as the analyte detector and reporter, respectively; for example, CD7-FITC denotes anti-CD7 as the analyte detector and FITC as the analyte reporter. Individual antibody catalogue numbers were not available in the accessible clinical laboratory records; all available reagent information is provided below. Isotype controls were used for gate setting and compensation. Lymphocytes were gated according to CD45/side-scatter characteristics, followed by analysis of abnormal B-cell populations, light-chain restriction and lineage-associated markers. Representative flow cytometry dot plots/histograms with population frequencies are shown in Fig. 2. The following antibody panels were used: i) IgG1-FITC/IgG1-PE/IgG1-PerCP/IgG1-APC/IgG1-PE-Cy7/IgG1-APC-Cy7/IgG1-V450/CD45-V500; ii) cIgG1-FITC/cIgG1-PE/cIgG1-PerCP/cIgG1-APC/cIgG1-PE-Cy7/IgG1-APC-Cy7/cIgG1-V450/CD45-V500; iii) CD7-FITC/CD117-PE/CD3-PerCP/CD4-PE-Cy7/CD5-APC/CD56-V450/CD8-APC-Cy7/CD45-V500/CD2-BV605; iv) κ-FITC/λ-PE/CD38-PerCP/CD19-PE-Cy7/CD10-APC/CD20-APC-Cy7/CD56-Pacific Blue/CD45-V500; v) CD16-FITC/CD117-PE/CD34-PerCP/CD33-APC/CD13-PE-Cy7/CD11b-Pacific Blue/HLA-DR-APC-Cy7/CD45-V500; vi) MPO-FITC/CD64-PE/CD34-PerCP/CD42a-APC/CD36-APC-Cy7/CD45-V500/CD14-BV421;vii)TdT-FITC/CD22-PE/CD34-PerCP/cCD3-APC/CD117-PE-Cy7/CD38-BV421/CD45-V500; viii) Ki-67-FITC/CD103-PE/CD19-PE-Cy7/CD79b-APC/CD72-Pacific Blue/CD45-V500; and ix) FMC7-FITC/CD23-PE/CD200-PE-Cy7/CD11c-APC/CD19-Pacific Blue/CD45-V500.

Pathological and immunohistochemical staining protocol. Pathological and immunohistochemical examinations were performed according to routine clinical diagnostic pathology procedures. Fine-needle aspiration smears from the thyroid nodule and supraclavicular lymph node were immediately fixed in 95% ethanol at room temperature for 20 min following specimen acquisition. For immunohistochemical staining, paraffin-embedded sections were used; no fresh-frozen sections were used. Sections were cut at 4 μm. Available cytological or tissue sections were deparaffinized when applicable, rehydrated, subjected to antigen retrieval, and treated with 0.04% hydrogen peroxide to block endogenous peroxidase activity. No serum or protein blocking reagent was used. Primary antibodies were used as ready-to-use reagents compatible with the automated immunohistochemical staining platform, and no manual antibody dilution was performed. Primary antibody incubation and secondary antibody detection were performed using an automated immunohistochemical staining system (BenchMark ULTRA PLUS, Roche Diagnostics) according to the manufacturer's routine clinical protocol. Detection was performed using the VENTANA OptiView DAB IHC Detection Kit (Roche Diagnostics; cat. no. no. 760-700), followed by chromogenic visualization with diaminobenzidine and hematoxylin counterstaining. Individual antibody catalogue numbers, as well as exact incubation times and temperatures, were not available in the accessible clinical pathology records because staining was performed using platform-specific ready-to-use reagents under a standardized automated workflow. Appropriate positive and negative controls were included. Whole-section scanned images were acquired using a Motic EasyScan digital slide scanning and application system and reviewed using Motic DSAssistantLite software (Motic VM V1 Viewer 2.0). Scale bars are provided in the corresponding figure legends.

For the thyroid nodule, the immunohistochemical panel included CK19, galectin-3, HBME-1, CD56 and Ki-67. For the supraclavicular lymph node, the immunohistochemical panel included CD20, CD79a, BCL-2, LEF-1, MUM-1, CD5, CD23, Cyclin D1, SOX11, CD3, CD10, CD21, CD30, c-Myc, BCL-6, myeloperoxidase, terminal deoxynucleotidyl transferase, anaplastic lymphoma kinase and Epstein-Barr virus-encoded small RNAs.