haematologica
Journal of the Ferrata Storti Foundation

Purrfect mimicry: cat scratch disease mimicking Richter transformation in chronic lymphocytic leukemia

by Jan A. Burger, Roberto N. Miranda and Javier A. Adachi

Received: September 11, 2026.
Accepted: November 17, 2026.

Citation: Jan A. Burger, Roberto N. Miranda and Javier A. Adachi. Purrfect mimicry: cat scratch disease mimicking Richter transformation in chronic lymphocytic leukemia.
Haematologica. 2026 Nov 26. doi: 10.3324/haematol.2026.301984 [Epub ahead of print]

Publisher's Disclaimer.
E-publishing ahead of print is increasingly important for the rapid dissemination of science.
Haematologica is, therefore, E-publishing PDF files of an early version of manuscripts that have completed a regular peer review and have been accepted for publication.
E-publishing of this PDF file has been approved by the authors.
After having E-published Ahead of Print, manuscripts will then undergo technical and English editing, typesetting, proof correction and be presented for the authors' final approval, the final version of the manuscript will then appear in a regular issue of the journal.
All legal disclaimers that apply to the journal also pertain to this production process.

Purrfect mimicry: cat scratch disease mimicking Richter transformation in chronic lymphocytic leukemia

By Jan A. Burger[1], Roberto N. Miranda[2], and Javier A. Adachi[3]

[1]Department of Leukemia, [2]Department of Hematopathology, and [3]Department of Infectious Diseases, The University of Texas, M.D. Anderson Cancer Center, Houston, TX, USA

Author's contributions: JAB: conceptualization, clinical care of the patient, data collection, writing and editing. RNM: histopathological review and interpretation, writing and editing. JAA: clinical management, data interpretation, writing and editing.

Author's disclosures: The authors declare that they have no relevant financial or non-financial competing interests related to the subject matter of this manuscript.

Acknowledgment: This work received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. Institutional support was provided by the Department of Leukemia, The University of Texas MD Anderson Cancer Center.

Artificial intelligence declaration: No generative artificial intelligence tools were used in the preparation of this manuscript.

Data sharing statement: De-identified data may be available from the corresponding author upon reasonable request and with appropriate institutional approval.

Correspondence: Jan A. Burger, MD, PhD, Department of Leukemia, The University of Texas MD Anderson Cancer Center, Unit 428, PO Box 301402, Houston, TX 77230-1402, USA; Phone: 713-563-1487; E-mail: jaburger@mdanderson.org

Case Report

In 2020, a 44-year-old female presented to our clinic with suspected Richter transformation from chronic lymphocytic leukemia (CLL). This case report was prepared in accordance with the ethical principles of the Declaration of Helsinki. This is a publication of a single de-identified case based on routine clinical care and all identifying patient information has been omitted. The patient provided written informed consent for publication of this case report, including clinical details, laboratory data, imaging findings, and any accompanying images. A signed copy of the consent form is retained by the authors and will be made available upon request.

The patient had a history of CLL since 2011, her CLL risk factors include 13q deletion by FISH cytogenetics, unmutated IGHV, and ATM, TP53, SF3B1 and XPO1 mutations by targeted sequencing. She initially received rituximab and methyl prednisone treatment and then transitioned to long-term ibrutinib treatment in 2015, initially at 420 MG daily, and dose-reduced to 140 MG in 2017. In early December 2020 she noted swelling of her submandibular lymph nodes, her local oncologist in Peru recommended a comprehensive workup, and she decided to come to MD Anderson Cancer Center for her further evaluation. Upon arrival in our clinic, we noted submental lymph node swelling with individual lymph nodes measuring approximately 3-4 cm that were mildly tender to touch. The peripheral blood workup was largely within normal limits, her ANC was 7.02, ALC 3.99, the lactate dehydrogenase (LDH) was normal, and she had no B symptoms or other symptoms besides her lymphadenopathy. PET CT demonstrated multiple enlarged submental/submandibular lymph nodes with high standardized uptake values (SUV) of up to 16.8, an activity significantly greater than expected for CLL, raising concern for Richter transformation (Figure 1A). No other areas of active CLL were noticed. The patient underwent lymph node biopsy, which demonstrated CD79a-positive CLL cells (Figure 1B) and an inflammatory infiltrate, with presence of CD68-positive histiocytes (Figure 1C) admixed with neutrophils and presence of ill-defined granulomas not meeting criteria for suppurative granulomas. In-situ hybridization for Epstein-Barr virus RNA (EBER) and the Warthin-Starry (WS) stain, a silver nitrate-based histological stain used to identify Bartonella henselae, were negative. The more detailed history revealed that the patient's elderly cat became unconscious 2 months prior to her development of lymphadenopathy, and the patient successfully resuscitated the cat, including mouth-to-mouth ventilation, and while regaining consciousness the cat bit the patient's lower lip, followed by a week-long time of local irritation and swelling to her lower lip. Her serology for Bartonella henselae came back IgG positive (titer: 1:256) and IgM negative, suggesting a diagnosis of "cat-scratch" disease (Bartonella lymphadenitis). She started on azithromycin 500 mg orally the first day, followed by 250 mg daily for 4 additional days, and her lymphadenopathy with time resolved. The patient regularly returns for annual

follow-up visits to our clinic, last in September 2026, and continues to be in a durable remission on long-term ibrutinib therapy.

Cat scratch disease (CSD) is a relatively common zoonotic infection acquired from cats, who can carry B. henselae, a fastidious gram-negative bacterium, in their blood, saliva, and on their claws[1]. Cat fleas are the main vector that maintains and spreads the bacteria among cats. The most common clinical presentation of CSD is lymphadenopathy proximal to the site of inoculation with or without fever, weight loss, and systemic involvement. The differential diagnosis for rapidly enlarging FDG-avid lymphadenopathy in a patient with long-standing CLL on BTK inhibitor therapy is broad and clinically consequential. True Richter transformation, most commonly to diffuse large B-cell lymphoma (DLBCL) is characterized by aggressive clinical features including bulky or asymmetrically enlarging nodes, B symptoms (fever, night sweats, weight loss), cytopenias, and markedly elevated LDH. On PET-CT, SUVs often exceed 10–15, reflecting high metabolic activity[2]. Histologically, Richter transformation demonstrates sheets of large neoplastic B cells with high mitotic activity, loss of CLL markers such as CD5/CD23 in many cases, and clonal relationship to the underlying CLL in most cases. Other important differentials include accelerated CLL, where proliferation centers expand without full large-cell transformation; this can produce intermediate histologic features and elevated SUVs[3]. Viral infections, particularly herpes simplex virus (HSV)- and Epstein-Barr virus (EBV)-related lymphoproliferations[4],[5] are recognized mimics in CLL patients, especially those exposed to fludarabine or other T-cell-depleting agents and can present with similar nodal enlargement. Other infectious causes such as mycobacterial infections, nocardiosis, toxoplasmosis, or fungal disease enter the differential, particularly in immunosuppressed hosts, but usually feature more granulomatous or necrotizing patterns and systemic signs[6].

In this patient, the isolated submandibular/submental involvement, absence of B symptoms, normal LDH, preserved blood counts, and tender rather than rock-hard nodes already indicated that the patient lacked typical clinical signs of Richter transformation. The history of a cat bite during resuscitation provided the crucial epidemiologic clue, redirecting attention to zoonotic infection. Bartonella henselae infection fits because the inoculation site (lower lip) drained to the affected nodal basin, and the timeline, approximately two months from bite to lymphadenopathy, aligns with the typical subacute course of CSD. The resolution with a brief azithromycin course, a commonly used standard therapy for CSD with lymphadenitis, and sustained remission over five years on continued ibrutinib underscore the reversibility of such mimics when correctly identified.

The negative Warthin-Starry (WS) stain and negative EBER in this case merit further discussion. The Warthin-Starry silver stain is a traditional method to visualize the small, pleomorphic gram-negative rods of Bartonella henselae, which appear as black bacilli in clusters or chains, often extracellular in necrotic areas or near the nodal capsule.

However, its sensitivity is limited, and it performs less reliably in subacute or resolving infections when bacterial load diminishes. A study showed that immunohistochemistry for B. henselae outperforms WS alone and combining both modalities increases overall detection to almost 98%[7]. In this instance, the negative WS does not exclude CSD, especially given the serologic detection of Bartonella henselae IgG antibodies and clinical resolution with azithromycin; the infection may have been at a stage with low organism burden, or the bacteria may have been sparse in the sampled tissue. Similarly, the IgM-negative serology with IgG positivity (titer 1:256) supports the presumed diagnosis of CSD given the longer time that passed between cat bite and blood draw for the CSD serology. IgM antibodies typically appear early in acute infection but are often transient, waning within weeks to a few months, and may be absent by the time lymphadenopathy becomes prominent or prompts medical evaluation. In contrast, IgG rises later (2–4 weeks post-exposure) and can persist for months to years, reflecting convalescent or recent infection. Many validated cases of CSD, particularly in adults or subacute presentations, show isolated IgG elevation or high IgG titers without detectable IgM. Serologic testing by indirect immunofluorescence assay (IFA) has variable performance, with IgM sensitivity around 89% in some pediatric systemic cases but lower overall; specificity remains high, and background seropositivity in the general population is low (2–6%). In immunocompromised patients on ibrutinib, humoral responses may be blunted[8], further favoring IgG-dominant patterns. When clinical suspicion is high, as here with compelling exposure history and compatible histology (mixed inflammatory infiltrate with histiocytes, neutrophils, and plasma cells without large-cell sheets), IgG positivity at a significant titer supports the diagnosis even with negative IgM. Molecular testing such as PCR on tissue would offer higher specificity if available, though it was not pursued once serology and response to therapy supported the etiology.

This case fits within a broader pattern of zoonotic infections masquerading as malignancy progression in immunocompromised hosts. The first documented instance of cat scratch disease mimicking Richter syndrome in CLL dates to 2005[9], when a patient with recent CLL diagnosis presented with rapidly enlarging nodes, constitutional symptoms, and initial suspicion of high-grade transformation; biopsy instead showed granulomatous features consistent with Bartonella, later verified serologically. Subsequent reports include a recent description of a young Asian female with CLL on zanubrutinib who developed confirmed Bartonella lymphadenitis diagnosed via next-generation sequencing[10]. Larger institutional experiences further contextualize the risk. A recent review from MD Anderson identified multiple cases of cat scratch disease mimicking malignancy across hematologic and solid cancer patients[11], noting that Bartonella can produce PET-positive adenopathy indistinguishable from lymphoma on imaging alone, often requiring biopsy and serologic correlation for definitive differentiation. Fitting with our case, the authors noted that most patients were young,

female, had prior cat exposure, and had no systemic symptoms. Regional lymphadenopathy was the most common finding.

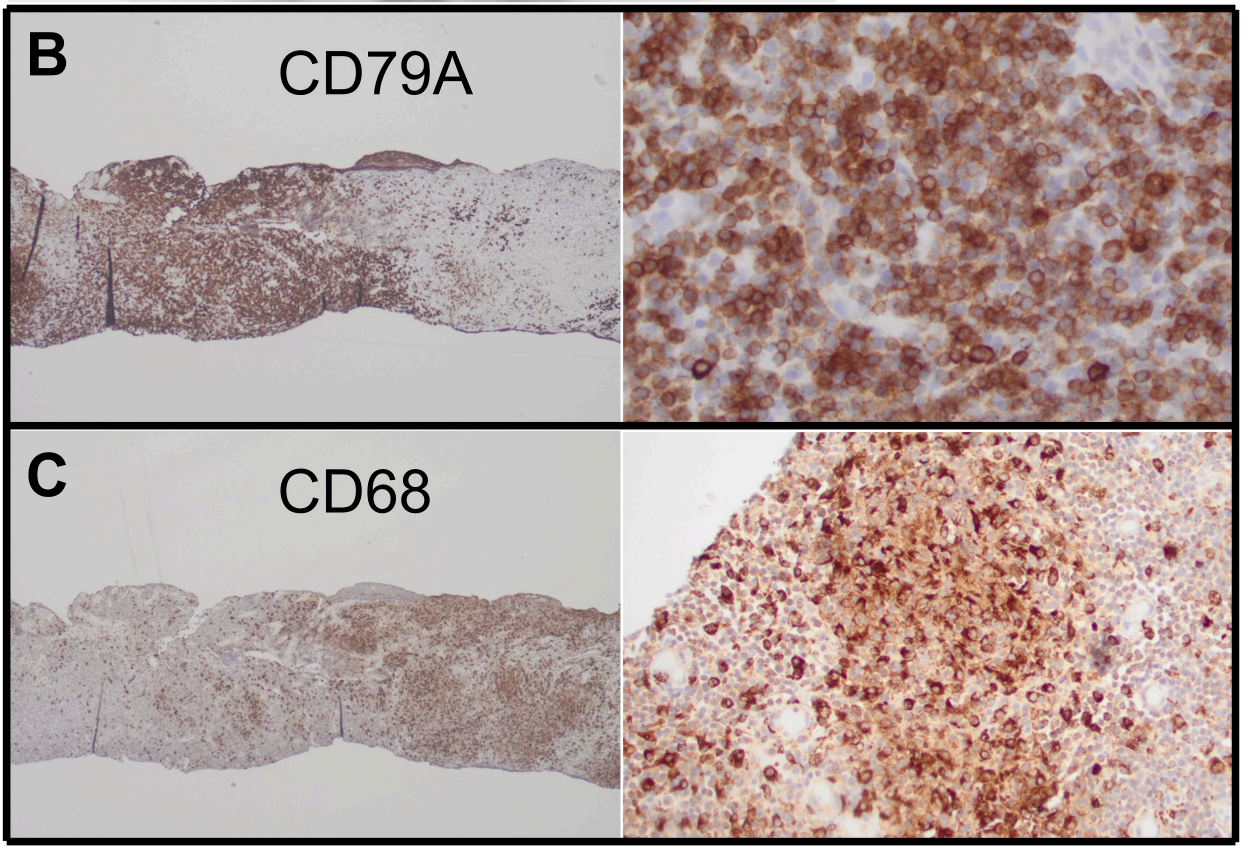
In summary, these cases underscore several key lessons for CLL management. First, zoonotic exposures warrant explicit inquiry in any unexplained nodal flare, particularly when confined to drainage areas of potential inoculation sites. Second, while Richter transformation remains a feared complication occurring in a minority of CLL patients and typically accompanied by systemic signs, elevated LDH, and more widespread disease, infectious mimics like Bartonella lymphadenitis are treatable and reversible, highlighting the value of maintaining a broad differential even in high-risk CLL patients. Finally, the excellent long-term outcome in this and similar patients illustrates how vigilant exclusion of benign infectious etiologies prevents overtreatment and preserves quality of life amid ongoing CLL-directed therapy. Awareness of these overlaps continues to refine diagnostic algorithms, emphasizing multimodal evaluation, clinical history, advanced imaging interpretation, targeted biopsy review, and microbiologic testing, over reflexive assumptions of malignancy progression.

References

1. Nelson CA, Saha S, Mead PS. Cat-scratch disease in the United States, 2005-2013. Emerg Infect Dis. 2016;22(10):1741-1746.
2. Kittai AS, Marchetti M, Al-Sawaf O, et al. International consensus statement on diagnosis, evaluation, and research of Richter transformation: the ERIC recommendations. Blood. 2025;146(3):291-303.
3. Gine E, Martinez A, Villamor N, et al. Expanded and highly active proliferation centers identify a histological subtype of chronic lymphocytic leukemia ("accelerated" chronic lymphocytic leukemia) with aggressive clinical behavior. Haematologica. 2010;95(9):1526-1533.
4. Chang A, Sholukh AM, Wieland A, et al. Herpes simplex virus lymphadenitis is associated with tumor reduction in a patient with chronic lymphocytic leukemia. J Clin Invest. 2022;132(18):e161109.
5. Jain P, Burger JA, Khoury JD. CLL progression after one cycle of FCR: richter's transformation versus EBV-associated lympho-proliferation. Am J Hematol. 2017;92(10):1113-1114.
6. Parikh SA, Bhusal Y, Faderl SH, et al. The great imitator: systemic nocardiosis mimicking Richter's transformation in relapsed chronic lymphocytic leukemia. J Clin Oncol. 2010;28(35):e732-734.
7. Peng J, Fan Z, Zheng H, Lu J, Zhan Y. Combined application of immunohistochemistry and warthin-starry silver stain on the pathologic diagnosis of cat scratch disease. Appl Immunohistochem Mol Morphol. 2020;28(10):781-785.
8. Pleyer C, Sun C, Desai S, et al. Reconstitution of humoral immunity and decreased risk of infections in patients with chronic lymphocytic leukemia treated with Bruton tyrosine kinase inhibitors. Leuk Lymphoma. 2020;61(10):2375-2382.
9. Razaq M, Godkar D, Mankan N, Sridhar S, Hussain S, Ohri A. Cat scratch disease mimicking Richter's Syndrome in a patient with chronic lymphocytic leukemia. Leuk Lymphoma. 2005;46(3):443-445.
10. Luan C, Yang X, Dong L, Zhu Y, Zhao H. Chronic lymphocytic leukemia young patient in steady state on zanubrutinib diagnosed with cat scratch disease via next-generation sequencing. Mediterr J Hematol Infect Dis. 2026;18(1):e2026007.
11. Dhal U, Hicklen RS, Tarrand J, Kontoyiannis DP. Cat scratch disease as a mimicker of malignancy. Open Forum Infect Dis. 2021;8(11):ofab500.

Figure 1: PET CT imaging and lymph node biopsy findings in a CLL patients with Cat Scratch Disease. (A) PET-CT showing high SUV submandibular lymphadenopathy in a CLL patient after cat bite into the lower lip. (B) CLL on the left half of the core biopsy involving a cervical lymph node. The B-cell marker CD79a shows that most lymphocytes express CD79a, weakly reactive, consistent with SLL/CLL. CD79a with hematoxylin counterstain, 40x (left hand panel), 400x (right hand panel). (C) Needle core biopsy displaying a diffuse histiocytic infiltrate on the right half of the biopsy. CD68 immunohistochemistry with hematoxylin counterstain, 40x. (left hand panel). The histiocytic cell marker CD68 shows that most cells are positive, with vaguely nodular pattern, suggestive of granuloma (right hand panel, 400x).


A
S


B
CD79A
C
CD68