Oncology, Nuclear Medicine and Transplantology

Case Report

Hodgkin's Lymphoma as a Rare Variant of Richter's Syndrome in Chronic Lymphocytic Leukemia: A Clinical Case Description

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Abstract:
Richter's syndrome (RS) is a malignant transformation of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) into a more aggressive lymphoid neoplasm. Typically, this term refers to the development of diffuse large B-cell lymphoma (DLBCL), which accounts for 90-95% of transformations. Much more rarely (in less than 5% of cases), the so-called Hodgkin's variant of Richter's syndrome occurs—transformation into classical Hodgkin's lymphoma (HL). [1] The Hodgkin's variant is characterized by the appearance of Reed-Sternberg cells or their variants in the infiltrate, surrounded by an inflammatory background typical of HL. It most often develops in patients with a long history of CLL/SLL, sometimes in the context of immunosuppression or after treatment with purine analogs and monoclonal antibodies. [2] The clinical picture of the Hodgkin's variant of Richter's syndrome typically includes pronounced B-symptoms (fever, night sweats, weight loss), rapidly progressing enlargement of lymph nodes and/or splenomegaly. Unlike the DLBCL variant, the course may be somewhat less aggressive; however, the prognosis remains unfavorable compared to primary Hodgkin's lymphoma. [3]

Keywords: Chronic Lymphocytic Leukemia (CLL); Hodgkin's Lymphoma; Richter's Transformation; Venetoclax; Bruton Tyrosine Kinase Inhibitors (BTK Inhibitors); BV-AVD

Introduction

Richter's syndrome (RS) is a malignant transformation of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) into a more aggressive lymphoid neoplasm. Typically, this term refers to the development of diffuse large B-cell lymphoma (DLBCL), which accounts for 90-95% of transformations. Much more rarely (in less than 5% of cases), the so-called Hodgkin's variant of Richter's syndrome occurs—transformation into classical Hodgkin's lymphoma (HL). [1]

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The clinical picture of the Hodgkin's variant of Richter's syndrome typically includes pronounced B-symptoms (fever, night sweats, weight loss), rapidly progressing enlargement of lymph nodes and/or splenomegaly. Unlike the DLBCL variant, the course may be somewhat less aggressive; however, the prognosis remains unfavorable compared to primary Hodgkin's lymphoma. [3]

Diagnosis is confirmed through histological and immunohistochemical examination of the lymph node biopsy or affected organ. Treatment involves chemotherapy regimens typically used for Hodgkin's lymphoma (ABVD, BEACOPP, etc.), often combined with antiviral or targeted therapy. In cases of resistant forms, autologous or allogeneic hematopoietic stem cell transplantation may be considered. [3] [4]

This clinical case illustrates the rare variant of Richter's syndrome with transformation into Hodgkin's lymphoma, demonstrating the challenges in diagnosis, differential assessment of morphological changes, and the choice of optimal treatment strategy for patients with CLL.

Clinical Case

Patient M., born in 1958, has been under observation since 2009 for chronic lymphocytic leukemia, diagnosed based on morphological, immunological, and clinical-hematological data. During the observation, several lines of therapy were administered, including:

- Chemotherapy with FC and RFC regimens;
- Monoclonal immunotherapy with rituximab;
- Since 2020—targeted therapy with Bruton's tyrosine kinase inhibitor (ibrutinib 420 mg/day) due to the presence of deletion 17p13 (del(17p)).

On the background of ibrutinib therapy, stable disease control was achieved. However, in the spring of 2025, the patient showed clinical and laboratory deterioration: enlargement of peripheral lymph nodes (right axillary lymph nodes up to 2.6×1.3 cm, 1.4×0.5 cm, and 1.2×0.5 cm, left up to 1.2×0.6 cm, 1.6×0.5 cm; inguinal lymph nodes: right up to 1.3×0.3 cm, 0.6×0.4 cm, 1.1×0.4 cm, left up to 1.2×0.4 cm, 1.4×0.4 cm), increase in lymphocytosis, appearance of B-symptoms (night sweats, low-grade fever), as well as splenomegaly.

The patient was admitted to the LLP "National Scientific Oncology Center" in the Department of Lymphoproliferative Diseases, where on April 16, 2025, an excision of the left axillary lymph node was performed to exclude Richter's transformation. Given the disease progression, combined therapy was started: venetoclax (BCL-2 inhibitor) in combination with continued ibrutinib therapy.

Diagnosis of Transformation

Histological and immunohistochemical examination confirmed the diagnosis of Richter's transformation into classical Hodgkin's lymphoma (CHL-RT). The histological report showed a picture of a B-cell lymphoma of small lymphocytes (CLL/SLL) with areas morphologically resembling classical Hodgkin's lymphoma, containing Hodgkin and Reed-Berezovsky-Sternberg (RB-S) cells.

Immunohistochemically, small cells expressed CD20, PAX5, CD5, and CD23, while large Hodgkin-type cells were positive for CD30 and PAX5 but negative for CD20. These findings confirmed the diagnosis of CLL/SLL transformed into Hodgkin's lymphoma.

Due to the rarity of Hodgkin-like transformation, the material was sent for a second opinion to the reference laboratory of the Federal State Budgetary Institution "NMIC Hematology" of the Ministry of Health of the Russian Federation, Moscow, where the conclusion was confirmed. The results of the secondary examination: the morphological picture of the lymph node is characterized by a focal-diffuse lymphoid infiltrate of small cells with signs of proliferative activity and areas of fibrous tissue containing Hodgkin and Reed-Berezovsky-Sternberg cells.

Treatment

Venetoclax therapy is effective against CLL but does not affect Hodgkin's lymphoma cells. Considering the presence of a dual hematologic substrate (CLL and CHL-RT), the possibility of adding chemotherapy with the BV-AVD regimen (brentuximab vedotin + doxorubicin, vinblastine, dacarbazine) [2,3] was considered.

Unfortunately, PET-CT was not performed before the start of treatment due to limitations in the availability of this procedure and the rapid progression of the disease.

Given the aggressive course of the disease, a decision was made to begin combined therapy with venetoclax + BV-AVD as a potentially effective option. Ibrutinib was discontinued after escalating the dose of venetoclax within the planned regimen.

From June 13 to June 27, 2025, the first course of the regimen was administered. No complications were noted during hospitalization. A repeat course of BV-AVD is planned, after which treatment efficacy will be evaluated using PET-CT.

Discussion

Richter's syndrome (RS) is the transformation of CLL into a more aggressive malignant disease, characterized by rapid progression and often limited response to treatment. The key method for diagnosing RS is histopathological examination. The most common form of RS is DLBCL, found in 2-8% of patients with CLL. However, other transformation variants are described in the literature, including T-cell lymphomas, multiple myeloma, Burkitt lymphoma, and lymphoblastic lymphoma.

The Hodgkin's variant of transformation occurs in less than 1% of RS cases. To date, about 100 confirmed observations of CHL-RT have been published in the literature. Two histological types of HL in CHL-RT are distinguished:

- Type I—Reed-Sternberg cells are scattered or grouped against the typical CLL infiltrate background.
- Type II—Reed-Sternberg cells are found on a polymorphic reactive background, making the picture indistinguishable from de novo Hodgkin's lymphoma.

The most common histological subtype of HVRT is the mixed-cell variant, followed by nodular sclerosis, lymphocytic depletion, and lymphocytic predominance. [5–8]

Our clinical case corresponds to Type I: in several sections of the small-cell lymphoid infiltrate, nodular-like structures with stromal fibrosis are identified, represented by small lymphoid cells, fibroblasts, histiocytes, and plasma cells. Among them, individual large Hodgkin and Reed-Sternberg cells are detected.

Despite the availability of various chemotherapy regimens, the treatment of CHL-RT remains a challenging task, and the prognosis is worse than for primary Hodgkin's lymphoma. Literature describes combined regimens directed at HL: ABVD, BEACOPP, CHOP ± R, CVPP [7–9]. Patients achieving complete remission remain under observation until disease progression; in the absence of complete remission, regimens for refractory HL are considered, as well as the possibility of non-myeloablative allogeneic hematopoietic stem cell transplantation in the first remission.

Promising therapy directions include the use of anti-EBV agents and monoclonal antibodies against CD30 (brentuximab vedotin), but the results are still limited. Overall, the response to treatment and clinical outcomes in CHL-RT are worse than for de novo HL but better than for the DLBCL variant of RS.

In our case, the patient tolerated the first course of chemotherapy well, feels good, and remains under observation until the second course is completed, after which treatment response will be evaluated.

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References

1. Gupta N, Mittal A, Duggal R, Dadu T, Agarwal A, Handoo A. Hodgkin Variant of Richter's Transformation in Chronic Lymphocytic Leukemia (CLL): An Illustrative Case Report and Literature Review. Int J Hematol Oncol Stem Cell Res. 2021 Oct 1;15(4):249-54. doi: 10.18502/ijhoscr.v15i4.7480.

2. Stephens DM, Boucher K, Kander E, Parikh SA, Parry EM, Shadman M, et al. Hodgkin lymphoma arising in patients with chronic lymphocytic leukemia: results from a large multi-center collaboration. Haematologica. 2021 Nov 1;106(11):2845-52. doi: 10.3324/haematol.2020.256388.
3. Krause JR, Drinkard LC, Keglovits LC. Hodgkin lymphoma transformation of chronic lymphocytic leukemia/small lymphocytic lymphoma. Proc (Bayl Univ Med Cent). 2013 Jan;26(1):16-8. doi: 10.1080/08998280.2013.11928901.
4. Zhu K, Jamroz A, Huang S, Villa D, Freeman CL, Scott DW, et al. Outcomes of Hodgkin variant Richter transformation in chronic lymphocytic leukaemia and small lymphocytic lymphoma in British Columbia. Br J Haematol. 2022 Aug;198(4):684-92. doi: 10.1111/bjh.18241.
5. Mao Z, Quintanilla-Martinez L, Raffeld M, Richter M, Krugmann J, Burek C, et al. IgVH mutational status and clonality analysis of Richter's transformation: diffuse large B-cell lymphoma and Hodgkin lymphoma in association with B-cell chronic lymphocytic leukemia (B-CLL) represent 2 different pathways of disease evolution. Am J Surg Pathol. 2007 Oct;31(10):1605-14. doi: 10.1097/PAS.0b013e31804bdaf8.
6. Agrawal P, Bal A, Das A, Sachdeva M, Prakash G. Chronic Lymphocytic Leukemia With Hodgkin and Reed-Sternberg (HRS) Cells: A Potential Diagnostic Pitfall in Lymph Node Biopsies. Appl Immunohistochem Mol Morphol. 2017 Jan;25(1):e9-e11. doi: 10.1097/PAI.0000000000000345.
7. Bockorny B, Codreanu I, Dasanu CA. Hodgkin lymphoma as Richter transformation in chronic lymphocytic leukaemia: a retrospective analysis of world literature. Br J Haematol. 2012 Jan;156(1):50-66. doi: 10.1111/j.1365-2141.2011.08907.x.
8. Tsimberidou AM, O'Brien S, Kantarjian HM, Koller C, Hagemeister FB, Fayad L, et al. Hodgkin transformation of chronic lymphocytic leukemia: the M. D. Anderson Cancer Center experience. Cancer. 2006 Sep 15;107(6):1294-302. doi: 10.1002/cncr.22121.
9. Janjetovic S, Bernd HW, Bokemeyer C, Fiedler W. Hodgkin's lymphoma as a rare variant of Richter's transformation in chronic lymphocytic leukemia: A case report and review of the literature. Mol Clin Oncol. 2016 Mar;4(3):390-2. doi: 10.3892/mco.2016.727.