Richter Transformation Arising From Chronic Lymphocytic Leukemia

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This article presents a case of a patient diagnosed with an indolent form of chronic lymphocytic leukemia (CLL). He was being followed with close observation when he was diagnosed with Richter transformation, an aggressive lymphoma that develops from CLL. The development of Richter transformation carries a poor prognosis, in part, because of underlying molecular changes that give rise to the transformation. The prognosis also relates to the difficulty in the patient's ability to receive chemotherapy because of poor marrow reserves from the disease or the residual impact of prior treatments. Advanced practice nurses who follow patients with CLL need to be aware of the potential for Richter transformation.

AT A GLANCE

- Richter transformation, an aggressive form of lymphoma, is characterized by the rapid growth of lymphadenopathy, onset of B symptoms, extranodal disease, significant elevations of lactate dehydrogenase, and multiorgan dysfunction.
- Richter transformation may be treated with chemoimmunotherapy regimens, including the use of novel agents; allogeneic transplantation may be used in consolidation of the disease.
- By understanding Richter transformation, advanced practice nurses can initiate swift diagnosis and treatment for this condition.

KEYWORDS
Richter transformation; diffuse large B-cell lymphoma; chronic lymphocytic leukemia

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Chronic lymphocytic leukemia (CLL) is a low-grade lymphoproliferative disorder manifested by an elevated lymphocyte count of 5 x 10^9/L or greater. The abnormal lymphocytes express CD5, CD19, dimCD20, and CD23 (Parikh, 2018). Several prognostic markers help to stratify risk in CLL as indicated by the International Prognostic Index for CLL (see Table 1). On the International Prognostic Index for CLL, five factors have been shown to be associated with overall survival; the index is also used to predict time to first therapy in newly diagnosed, previously untreated CLL (Parikh, 2018). A 17p deletion (del17p) is associated with the least favorable prognosis and shortest overall survival (Parikh, 2018). Shorter time to first therapy, progression-free survival, and overall survival are also associated with *NOTCH1*, *SF3B1*, and tumor protein p53 (*TP53*) variants (Parikh, 2018; Rossi, Rasi, Fabbri, et al., 2012; Rossi et al., 2013).

Richter transformation, also known as Richter syndrome, is an aggressive form of lymphoma that develops in the background of CLL (Allan & Furman, 2019). Richter transformation occurs in about 2%–10% of CLL cases and is characterized by the onset of B symptoms (e.g., fevers, chills, drenching night sweats, weight loss), rapid growth of lymphadenopathy, extranodal disease (e.g., gastrointestinal tract, central nervous system, lungs, kidneys, skin), significant elevations of lactate dehydrogenase, and multiorgan dysfunction (from invasive or obstructive processes) (Petrackova et al., 2021). CLL itself can include lymphadenopathy as part of its characteristics; it is important to distinguish CLL lymphadenopathy from lymphadenopathy associated with Richter transformation because of treatment implications. The use of novel agents, such as Bruton tyrosine kinase inhibitors and B-cell lymphoma 2 inhibitors, are effective in CLL but not in Richter transformation (Allan & Furman, 2019). A biopsy is needed to confirm transformation. Positron-emission tomography–computed tomography can be used to determine the most likely site of transformation, with a standardized uptake value higher than other sites of disease (Allan & Furman, 2019).

Specific risk factors for the development of Richter transformation include *TP53* disruption, *NOTCH1* variations, cyclin-dependent kinase inhibitor 2A loss, and MYC activation (Allan & Furman, 2019). Independent risk factors for the development of Richter transformation include unmutated immunoglobulin heavy chain gene, Zeta-chain-associated protein kinase-70 expression, CD49d or CD38, telomere length, and genetic polymorphisms in CD38 and LRP4. The highest level of increased risk for the development of Richter