A New Look at an Old Syndrome

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The current standard therapies for chronic lymphocytic leukemia do not prevent Richter's transformation from occurring. If we are fortunate, new treatments will realize the hope that this usually fatal complication of chronic lymphocytic leukemia might be avoided.

In 1928, a pathologist at Bellevue Hospital in New York City named Maurice Richter performed an autopsy on a 46-year-old man. The patient had a 2-month history of abdominal pain and weight loss and was admitted to the hospital, where he died. He was found to have lymphatic leukemia and reticulum cell sarcoma.[1] In 1964, the term “Richter's syndrome” (or “Richter's transformation”) was introduced into the literature.[2] Subsequently, “Richter's transformation” has been used to describe not only the appearance of high-grade B-cell lymphoma in patients with chronic lymphocytic leukemia, but also transformation of any low-grade B-cell malignancy into a more aggressive disease. The phenomenon appears to occur most frequently in low-grade follicular lymphoma, but it can be seen in any small B-cell malignancy. Transformation does not have to be to diffuse large B-cell lymphoma; indeed, cases of the transformation of chronic lymphocytic leukemia to Hodgkin lymphoma, or to acute leukemia, are also reported using the phrase “Richter's transformation.”[3,4]

The incidence of transformation in chronic lymphocytic leukemia is generally described as being between 3% and 10%.[5,6] In follicular lymphomas, transformation from low-grade follicular lymphoma to diffuse large B-cell lymphoma is seen in 20% to 50% of patients clinically, and in a higher proportion of cases studied at autopsy.[7] As described in the article by Jain and O'Brien in this issue of ONCOLOGY, Richter's transformation has generally been associated with a poor prognosis. The few exceptions to this are typically patients in whom either (1) chronic lymphocytic leukemia (or another small B-cell malignancy) and diffuse large B-cell lymphoma appear to have developed simultaneously and are diagnosed simultaneously—or (2) the diffuse large B-cell lymphoma appears before the patient has been treated for chronic lymphocytic leukemia (or another indolent B-cell malignancy). In our institution's experience, the diffuse large B-cell lymphoma in patients in the above subsets frequently will respond to treatment such as R-CHOP (rituximab [Rituxan] plus cyclophosphamide, doxorubicin, vincristine, and prednisone) and can sometimes be “cured.” However, the small B-cell malignancy usually persists. Unfortunately, for patients who have been previously treated for chronic lymphocytic leukemia or another small B-cell malignancy, the appearance of diffuse large B-cell lymphoma usually has an ominous prognosis. As reported by Jain and O'Brien, the only patients likely to have long-term, disease-free survival are those in whom an allogeneic bone marrow transplant can be successfully completed.

For physicians who care for patients with chronic lymphocytic leukemia, it is important to consider Richter's transformation in those who have a change in their clinical status. The abrupt appearance of systemic symptoms such as fevers, sweats, weight loss, or rapid growth of lymph nodes in one (but usually not all) lymph node-bearing areas should raise the question of Richter's transformation. While a positron emission tomography (PET) scan can be useful in identifying an area with high uptake that would be an excellent site to biopsy, it is important that PET scanning not be used as a surrogate for biopsy. Richter's syndrome should be diagnosed histologically and not clinically. The excellent review by Jain and O'Brien in this issue of ONCOLOGY will be valuable to all physicians who might care for a patient with this unfortunate clinical event. However, it would be tremendously helpful if a way could be found to prevent Richter's transformation from occurring. The current standard therapies for chronic lymphocytic leukemia do not accomplish this. If we are fortunate, new treatments—perhaps the B-cell receptor inhibitors, such as ibrutinib and CAL-101—will realize the hope that this usually fatal complication of chronic lymphocytic leukemia might be avoided.

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References:

REFERENCES


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