



## Richter Syndrome: An Aggressive Transformation

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A 71-year-old male patient named M.R. was diagnosed with chronic lymphocytic leukemia (CLL). At the time of diagnosis, M.R. had generalized lymphadenopathy and splenomegaly, which caused him to experience significant abdominal discomfort. M.R. was treated with six cycles of fludarabine, cyclophosphamide, and rituximab (FCR), which is standard first-line chemotherapy, and tolerated this fairly well. His lymphadenopathy quickly resolved and, aside from mild nausea, had no complications from treatment.

Now, three years later, M.R. presented with a four-week history of malaise, fatigue, night sweats, and unintentional weight loss of 15 pounds. He was worried that his CLL was relapsing because his symptoms feel different than when he was diagnosed. He had no other comorbid conditions. On physical examination, M.R. appeared unwell. He had palpable cervical and submandibular lymph nodes (2–3 cm) and bilateral axillary lymphadenopathy measuring 5–6 cm. His white blood cell count was elevated, with an absolute lymphocyte count (ALC) of  $32.6 \times 10^9$  g/L. At his previous assessment three months prior, his ALC was  $10.4 \times 10^9$  g/L, indicating a lymphocyte doubling time of less than three months. His hemoglobin and platelets were 9.8 g/dl and 121,000 u/L, respectively, which was significantly lower anemia for M.R. with a stable platelet count. His lactate dehydrogenase (LDH) had always been within normal limits but had now increased to twice the upper limits of normal (590 u/L).

Positron-emission tomography/computed tomography (PET/CT) scan was performed on F-fluorodeoxyglucose and indicated a standardized uptake value (SUV) of 3–4 for the cervical and submandibular nodes and an SUV of

18 and 27 in the axillary nodes. M.R. was referred for an excisional biopsy of one of his axillary nodes. He did not understand why all of these tests were necessary and found the time waiting for appointments very difficult because he was eager to get started on treatment. The biopsy was performed a week later and he was sent home. One week later, M.R.'s oncologist told him that the pathology not only reported his underlying CLL, but also confirmed the presence of a more aggressive, diffuse large B-cell lymphoma (DLBCL), which would require treatment that was different from conventional CLL therapy. M.R. was not surprised by the findings; his doctor had explained that a Richter transformation was a potential outcome. M.R. was eager to start treatment.

A bone marrow biopsy was needed to complete staging, as well as a multi-gated acquisition scan to assess M.R.'s heart function before proceeding with anthracycline-based chemotherapy. He was started on rituximab, cyclophosphamide, vincristine, doxorubicin, and prednisone (R-CHOP), which is standard chemotherapy for DLBCL. Soon after starting treatment, M.R.'s night sweats ceased, the nodes began to shrink, and his appetite slowly returned. He did not lose any more weight but did experience some nausea from the chemotherapy and mild peripheral neuropathy to his feet. He and his wife were surprised by how much the loss of his hair affected him. He became more withdrawn and isolated with this round of chemotherapy, admitting that, this time, he really "felt like he was sick." He received a total of six cycles and, after completing his chemotherapy, M.R. was scheduled for a repeat PET/CT scan to assess treatment response. He was aware that the prognosis was poor if he had not responded to treatment but

was cautiously optimistic. The previous areas of lymphadenopathy had resolved, but a new retroperitoneal mass was found, measuring 3 x 5 cm, with an SUV of 6.3, which was concerning for disease progression. His advanced age excluded him from stem cell transplantation and he was started on a platinum-based, salvage chemotherapy regimen. M.R. and his wife then began discussions with the nurse and psychosocial clinicians about the uncertainty of their situation and their sense of hopelessness as they begin another round of chemotherapy.

### Richter Transformation

CLL is the most commonly diagnosed adult leukemia in the United States and Canada, with the average age at diagnosis being 71.5 years and with men diagnosed slightly more often than women (Jain & O'Brien, 2012). CLL is characterized by an accumulation and proliferation of phenotypically distinct monoclonal B-cell lymphocytes derived from the blood, marrow, or lymph nodes. Despite new understanding about the variable nature of the CLL disease trajectory, CLL is classified as an indolent, low-grade, lymphoproliferative disorder. In about 2%–10% of all cases, patients develop a more aggressive lymphoma known as Richter syndrome or Richter transformation (Parikh, Kay, & Shanafelt, 2014).

First described clinically by Maurice Richter in 1928, the term *Richter syndrome* was applied in the literature 40 years later to a subset of patients with CLL who developed large cell lymphoma (Lortholary et al., 1964). Richter syndrome is the transformation of CLL to an

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