A 70-year-old man was diagnosed with stage IVA follicular lymphoma grade 1 in 2005. He initially received rituximab treatment in 2006. In the next 5 years, he was enrolled in several clinical trials including Zevalin radioimmunotherapy in 2007. He was recently admitted due to a new onset of gastrointestinal bleeding. At admission, a complete blood count showed mild anemia, severe thrombocytopenia, and marked leukocytosis (31 × 10^9/L) attributed to increased circulating blasts. Bone marrow aspirate smear (panel A) and hematoxylin and eosin–stained biopsy section (panel B) demonstrated extensive involvement by the same blasts. These blasts had scant cytoplasm and reticulated chromatin. Whereas morphologically resembling lymphoblasts, they expressed surface CD10, CD19, and cytoplasmic λ immunoglobulin light chains. Whereas morphologically resembling lymphoblasts, they expressed surface CD10, CD19, and cytoplasmic λ immunoglobulin light chains. Fluorescence in situ hybridization (FISH) analyses (panels C-F) using break-apart (BAP) and dual fusion translocation (D-FISH) probes on the bone marrow identified 95% of nuclei with v-my c avian myelocytomatosis viral oncogene homolog (MYC)/immunoglobulin heavy chain (IGH) fusion, t(8;14); IGH/B-cell lymphoma 2 (BCL2) fusion, t(14;18); and a disruption of BCL6 and immunoglobulin λ chain (IGL), suggesting a BCL6/IGL fusion, t(3;22). The FISH abnormalities were verified by an abnormal karyotype: 46,XY,der(1)t(1;1)(p36.1;q25), der(3)t(3;22)(q27;q11.2),del(8)(q24.1),t(14;18)(q32;q21.3),add(22)(q11.2),add(22)(q13)(6].

The distinct cytogenetic abnormalities of MYC, BCL2, and BCL6 genes are consistent with a triple-hit lymphoma, a variant of BCL unclassifiable, with features intermediate between diffuse large BCL and Burkitt lymphoma. This patient died 6 weeks after the bone marrow biopsy.
A leukemic presentation of a "triple-hit" lymphoma

Dong Chen and Rhett P. Ketterling