Detection of t(14;18)(q32;q21) in B-Cell Chronic Lymphocytic Leukemia

Wolfgang Kern, MD; Torsten Haferlach, MD; Susanne Schnittger, PhD; Claudia Schoch, MD

- Cytomorphologic testing and multiparameter flow cytometry are the mainstays in diagnosing B-cell chronic lymphocytic leukemia, whereas fluorescence in situ hybridization that targets the translocation t(14;18)(q32;q21) often is used to identify follicular lymphoma. Therapy is highly diverse between both diseases. We describe a case with cytologically and immunologically proven B-cell chronic lymphocytic leukemia in which t(14;18)(q32;q21) was found. 

Arch Pathol Lab Med. 2005;129:410-411

Hematologic malignancies are diagnosed and classified according to recurring and characteristic findings in laboratory examinations. In general, cytologic testing, immunophenotyping, cytogenetics, and molecular genetics are used to identify specific disease subtypes in individual patients. An accurate diagnosis is essential for the management of most of these neoplasms, which in most cases is guided by the specific disease subtype.

B-cell chronic lymphocytic leukemia (B-CLL) is an indolent lymphatic malignancy that is diagnosed based on an abundance of lymphocytes in blood and bone marrow characteristically coexpressing CD19, CD20, CD23, and cyCD79a together with CD5 as revealed by cytomorphic testing and immunophenotyping. The immunologic distinction from the cytologically different mantle cell lymphoma, which also is a CD5+ B-cell neoplasm, is based on the negativity for CD22 and FMC7, a weaker expression of immunoglobulins, and the lack of CD103 expression. Other indolent B-cell lymphomas, including follicular lymphoma and marginal zone lymphomas, do not express CD5 and thus display a clearly distinct immunophenotype.

In B-CLL, modern diagnostics have revealed additional and prognostically highly relevant parameters. Among these, a major role has been demonstrated for fluorescence in situ hybridization (FISH), which is used for the detection of specific cytogenetic aberrations. The most common recurring aberrations are deletions of 11q, 13q, and 17p and trisomy 12. Based on these findings, the patient's prognosis can be estimated; therefore, the analysis is common practice at the time of diagnosis of the disease. In addition, FISH analysis of t(14;18)(q32;q21) is performed to rule out follicular lymphoma but may also be considered the only diagnostic measure in some cases.

In light of this context, we describe a patient with B-CLL carrying t(14;18)(q32;q21). The patient had no lymphadenopathy. Cytomorphologically, the cells were small mature lymphocytes without any indication of findings characteristic of follicular lymphoma, such as cleaved nuclei and the presence of 2 populations that differ in size (Figure 1). Accordingly, the immunophenotype revealed the characteristics of B-CLL with positivity for CD19, CD20, CD23, cyCD79a, HLA-DR, and CD5 and negativity for terminal deoxynucleotidyl transferase, CD22, CD10, FMC7, CD103, and myeloid and T-cell markers (Figure 2). There was a dim surface expression of immunoglobulins with light strain restriction to 1. FISH analysis (immunoglobulin heavy chain and Bcl-2) unequivocally identified the presence of a t(14;18) (Figure 3).

Although the frequently described occurrence of t(11;14) in B-CLL may be due to some similarity of the immunophenotypes of B-CLL and mantle cell lymphoma and resulting misinterpretation, there are only a small number of reported cases with B-CLL and t(14;18). The t(14;18) is considered highly specific for follicular lymphoma but has been found also in diffuse large cell lymphomas. The occurrence of t(14;18) in B-CLL has been described in 8 cases overall in all of which abnormal findings, such as the presence of small cleaved cells or the bright expression of immunoglobulins, were present, raising the question of whether true B-CLL cases have been analyzed. In contrast, t(14;18) has been identified in the present case, which exclusively has characteristics for B-CLL.

Therefore, this case argues in favor of applying a combination of methods for diagnosing indolent lymphomas and not to limit diagnostics to FISH analysis only to prevent misdiagnosis. The identification of additional cases with B-CLL and t(14;18) is needed to allow the definition
Figure 1. May-Grünwald-Giemsa staining showing small noncleaved lymphocytes and Gumprecht shadows (original magnification ×630).

Figure 2. Multiparameter flow cytometry showing coexpression of bright CD5 and CD20 (all cells shown in orange and pink are CD19+).

Figure 3. Fluorescence in situ hybridization analysis showing the colocalization for one probe pair against immunoglobulin heavy chain and Bcl-2 (original magnification ×1000).

of their biologic and clinical place within the group of indolent lymphomas.

References