

Leukaemia Section

Mini Review

Small lymphocytic lymphoma

Antonio Cuneo, Gian Luigi Castoldi

Hematology Section, Department of Biomedical Sciences, University of Ferrara, Corso Giovecca 203, Ferrara, Italy (AC)

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Clinics and pathology

Disease

Small lymphocytic lymphoma (SLL) represents the lymphomatous counterpart of B-cell chronic lymphocytic leukemia.

Phenotype/cell stem origin

The typical cases have faint surface IgM/IgD expression with k/l light chain restriction; pan-B antigens are positive, but CD22 expression is weak. CD5 and CD23 test positive, whereas CD10 and FMC7 are negative; the expression of CD11c and CD25 is variable; the postulated normal counterpart is a peripheral CD5+/CD23+ B cell; based on the presence/absence of the CD38 antigen, a distinction was suggested for CLL, that may potentially apply also to SLL, between virgin B-cells that have not encountered the antigen and cells harbouring somatic hypermutation of the Ig-gene variable region, corresponding to post-germinal memory-B cells.

Epidemiology

Accounts for 5-10% of NHL.

Clinics

The disease usually presents with bone marrow and peripheral blood (PB) involvement and typically runs an indolent course; transformation into diffuse large cell lymphoma (Richter's syndrome) may occur.

Pathology

Enlarged lymph nodes show an infiltrate consisting of a majority of small lymphocytes with clumped chromatin and inconspicuous nucleolus; larger cells (prolymphocytes and paraimmunoblasts) are also present, usually clustered in pseudo-follicles, referred to as "proliferation centres"; in some cases having the

histologic features of SLL, the cells may have plasmacytoid differentiation with cytoplasmic Ig and a paraprotein (monoclonal component) may be found in the serum; plasmacytoid differentiation, corresponding to many cases included in the category "immunocytoma, lymphoplasmacytoid type" in the Kiel classification does not constitute at the present time an indication of a different disease and should not be confused with the "lymphoplasmacytoid lymphoma", corresponding to most cases of Waldenstrom's macroglobulinemia, the prognostic impact of plasmacytic differentiation in SLL remains a subject for research.

Cytogenetics

Note

- Relatively few studies were performed on lymph node material; though it is reasonable to assume that a similar profile of molecular cytogenetic lesions may characterize SLL and CLL no formal proof that this is really the case was provided; data here summarized refer to those cases diagnosed as SLL and do not take into account the data described in CLL.
- A chromosome anomaly was detected by cytogenetics in 60-90% of the cases.

Cytogenetics morphological

Trisomy 12 was seen in 10-30% of the cases and other trisomies, involving chromosomes 3 (+3) and 18 (+18) in approximately 10% of the cases; Deletions/translocations 6q21-23 were detected in 15-25% of the cases and they showed a correlation with leukemic involvement by large prolymphocytoid cells; Structural changes of 11q, mostly deletions involving the q22-23 segment (del(11q)) were detected in 10-20% of the cases and structural anomalies of 12p13 in 10% of the cases in one study;

The t(14;19)(q32;q13.3), deletions/translocations 14q22 and the t(11,14)(q13;q32) were reported in several cases; other chromosome 14q32 translocations with 1p32 and other unknown partners may be found in SLL; in general, those cases with a 14q anomaly require a precise histologic characterization because their distinction from mantle cell lymphomas and marginal zone B-cell lymphomas may pose difficult diagnostic problems;

FISH studies found an approximate 50% incidence for cryptic 13q14 deletions and a 5-10% incidence for 17p13 deletions (advanced disease).

Cytogenetics molecular

Molecular cytogenetic lesions and methods for detection: the following associations were proposed:

6q21-q23: loss of a putative oncosuppressor gene; detection by FISH with 6q21 probe, CGH and LOH studies;

11q deletions: no study was specifically devoted to SLL; in CLL, ATM gene deletion with postulated loss of function in some cases; the most sensitive mean for detection is FISH with ATM-probes; SSCP and sequencing of exons with altered motility can be used for the demonstration of lesions of the remaining ATM allele;

13q14 deletions: putative oncosuppressor gene. FISH with probes mapping between the Rb and the D13S25 marker are ideal for the detection of small deletions. CGH is less sensitive;

17p13 deletions: loss of p53 function; detection is usually achieved by FISH with a p53 probe and SSCP and sequencing of exons with altered motility for the demonstration of lesions of the remaining allele;

t(14;19): fusion of IgH and BCL3 (transcription factor); the translocation exchanges chromosome bands similar in size and banding pattern; FISH with chromosome painting is useful; southern blotting detects most BCL3 rearrangements;

t(11;14)(q13;q32): fusion of IgH and BCL1/CCND1 (cyclin); dual-color FISH with BCL1 and IgH probes or

with probes proximal and distal to the BCL1 locus. PCR and southern blotting have limited application due to variability of the breakpoint location.

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