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Leukaemia Section

Mini Review

Splenic lymphoma with villous lymphocytes (SLVL)

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Clinics and pathology

Phenotype/cell stem origin

Light chain restriction surface immunoglobulin. Most cases express IgM and IgD. B-cells express CD19+, CD20+, CD22+, CD24+, CD79b+, FMC7+ and DBA44+. Lack expression of CD5 (85%), CD10, CD23, CD103 and CD123.

Epidemiology

In 1987, the term SLVL was introduced; 1-2% of non-Hodgkin lymphomas; occurs in the elderly (med 70 yrs); sex ratio 2M/1F.

Clinics

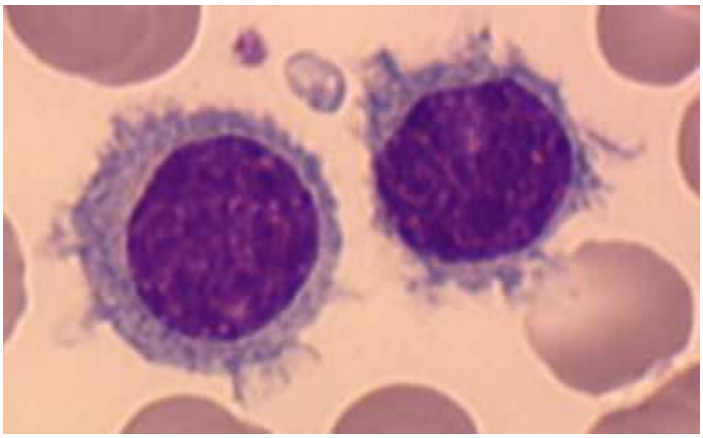
Splenomegaly without hepatomegaly nor enlarged lymph nodes; monoclonal Ig in a third of cases, autoimmune phenomena in 10% of patients, transformation to high grade lymphoma in 10% of cases.

Pathology

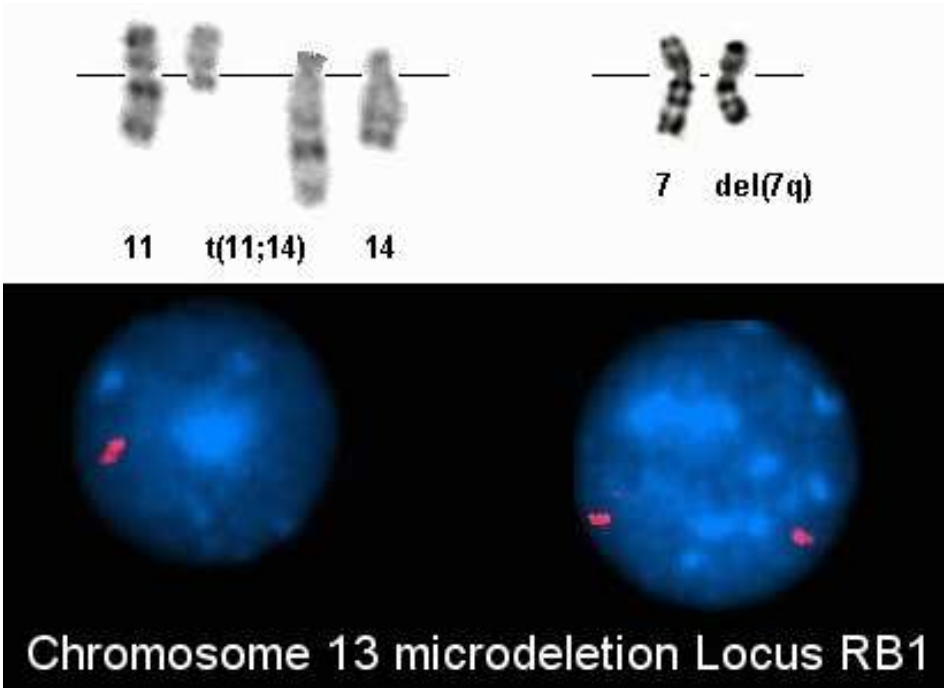
Spleen. Nodular replacement of the white pulp with a central core of small lymphocytes and larger cells in the peripheral marginal zone. Invasion of the splenic red pulp is inconstant. Bone marrow morphology showing intrasinusoidal lymphoma cells.

Treatment

Only in symptomatic patients: splenectomy or chemotherapy with purine analogues. Antiviral therapy (IFN) in patients with SLVL and hepatitis C.



Peripheral blood lymphocytosis in 75% of patients and villous lymphocytes on peripheral blood smears (Fig 1).



t(11;14)(q13;q32) R-Banding (top left); del(7q) (top right); 13q14 allelic loss at the RB1 locus deletion detected by interphase FISH (bottom).

Prognosis

Indolent B-cell malignancy with 5-yr survival: 80%; no consensus on adverse prognostic factors: WBC > 30 x 10^9/l, low lymphocyte count; cases treated with chemotherapy have shorter survival.

Cytogenetics

Cytogenetics morphological

A low mitotic activity is present in SLVL and most chromosomal banding analyses of SLVL have been based on cell cultures stimulated with different B-cell mitogens. The cytogenetic abnormalities are heterogeneous and often complex, with several recurrent abnormalities.

The most common abnormalities are those involving structural abnormalities of chromosome 7q22-q32 [20-40% of cases] in the form of translocation, mainly unbalanced, and 7q deletion (see Fig 2).

Some cases have been reported to show t(11;14)(q13;q32) [10-15%].

Structural abnormalities and microdeletion of 13q14 were found in 50% of cases. The 13q14 allelic losses at the RB1 locus deletion have been detected by interphase FISH.

Other abnormalities, in particular trisomy 3 [10-15%], i(17)(q10), t(6;14)(p21;q32) and 2p11 translocations, t(2;7)(p12;q21) were also observed in a few cases.

Immunoglobulin gene sequencing 43% of patients have an unmutated profile (>98% homology to the gem line sequence) and 57% of patients a mutated profile. Overuse of the VH1-2 gene segment is present in mutated and unmutaded cases.

Genes involved and proteins

Note

del(7q): gene unknown.

t(11;14)(q13;q32)BCL1 in 11q13 and IgH in 14q32 are involved in 20% of cases, with or without visible (11;14); BCL1 encodes the cyclin D1; role in the cell cycle control (G1 progression and G1/S transition); 5' BCL1 translocated on chromosome 14 near JH, resulting in promoter exchange; the immunoglobulin gene enhancer stimulates the expression of BCL1, and overexpression of BCL1 which accelerates passage through the G1 phase.

Trisomy 3: gene unknown but region 3q13.q32-q29 over-represented.

t(6;14)(p21;q32) cyclin D3 is located on 6p21 and, as CDK6, is implicated in the progression through the G1 phase of the cell cycle.

t(2;7)(p12;q21). CDK6 is located on 7q21 and dysregulation of CDK6 gene expression could be contribute to the pathogenesis of SLVL and SMZL.

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