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Leukaemia Section

Mini Review

Mantle cell lymphoma

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Clinics and pathology

Disease

NHL of the low to intermediate grade.

Phenotype / cell stem origin

B-cell lineage.

Epidemiology

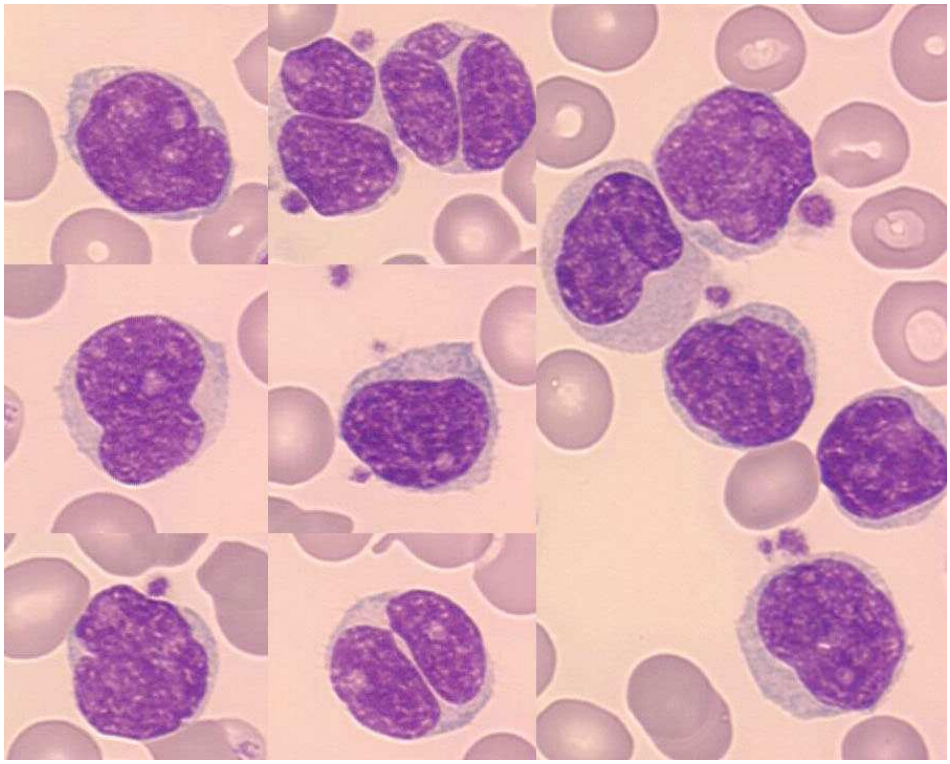
5% of NHL; sex ratio: 3M/1F; median age: 65 yrs.

Clinics

Advanced disease (Ann Harbor stage III-IV) with generalized lymphadenopathies in 90%, bone marrow involvement (70%), frequent splenomegaly (50%), hepatomegaly (30%), and gastro-intestinal involvement (20%), and lymphocytosis (30%); elevated LDH in 50%.

Pathology

Small cleaved cell B-lymphocytes with inconspicuous nucleoli and pale cytoplasm; with a pan B-cell, CD5+, CD10-, CD23- (in contrast with CLL) phenotype; diffuse, nodular and blastoid types, the latter having large cells and higher mitotic count.



Leukemic phase of mantle cell lymphoma. Peripheral blood. Small to medium sized lymphoid cells with slightly to markedly irregular nuclear contour. The nuclei have moderately dispersed chromatin bur inconspicuous nucleoli. From a patient with 46,XX,t(11;14)(q13;q32) - Courtesy Georges Flandrin.

Treatment

According to the age and the disease stage.

Prognosis

Median survival is 3 to 4 yrs; less than 2 yrs in the case of a leukaemic form (blastoid); in contrast with the good prognosis of the MALT lymphoma, a closely related disease.

Cytogenetics

Cytogenetics, morphological

Knowledge is still scarce, and data complex.
t(11;14)(q13;q32) is found in 50-70% of cases, but this translocation may also, at a much lesser frequency, be found in other diseases; the genes involved in this translocation are described below; t(11;14) is found in complex karyotypes.
Other frequent findings: deletion of parts of: 1p, 6q, 9p, 11q (in particular 11q22-23), 13q; gains of parts of: 3q, 8q, 15q; frequent markers; tetraploidy may be found, especially in the blastoid subtype.

Cytogenetics, molecular

CGH (compatrative genomic hybridization) may disclose important events in this disease, taken into account that the t(11;14) may be insufficient for oncogenesis; furthermore, this and other molecular cytogenetic techniques may come in addition to the usual techniques to 'dissect' complex karyotypes.

Genes involved and Proteins

BCL1

Location: 11q13

DNA / RNA

5 exons.

Protein

Encodes the cyclin D1; role in the cell cycle control: G1 progression and G1/S transition.

IgH

Location: 14q32

Results of the chromosomal anomaly

Hybrid gene

Description

5' BCL1 translocated on chromosome 14 near JH (junctions genes of IgH) and C in 3'; the breakpoint in BCL1 is in MTC (major translocation cluster), centromeric to the gene (in 5'), in 80% of cases, or dispersed in mTC1, 2, or 3 in 5' of the gene or in the 3' untranslated region of exon 5.

Fusion protein

Description

No fusion protein, but promoter exchange; the immunoglobulin gene enhancer stimulates the expression of BCL1.

Oncogenesis

Overexpression of BCL1 accelerates passage through the G1 phase.

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