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Prognostic factors in non-Hodgkin's lymphomas

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Molecular pathogenesis of germinal-center derived non-Hodgkin's lymphoma

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Non-Hodgkin's lymphoma (NHL) derive from mature B-cells (85% of cases) and in a minority of cases from T-cells. Most B-NHL types derive from germinal center (GO) or post-GO B-cells since they express various GO markers and have undergone hypermutation of IgV genes, a phenomenon apparently restricted to GO B-cells. The pathogenesis of NHL represents a multistep process, involving the clonal accumulation of genetic lesions that affect protooncogenes and tumor suppressor genes. The most common mechanism of genetic lesion is by chromosomal translocations, which alter the pattern of expression of various protooncogenes by juxtaposition of heterologous regulatory sequences. During the last 15 years, significant progress has been made in identifying the protooncogenes associated with various B-cell derived NHL subtypes. In fact, most B-cell derived NHL cases are associated with the deregulated expression by chromosomal translocation of various protooncogenes, including: i) BCL-2 in follicular lymphoma; ii) BOL-1 in mantle cell lymphoma; ii) C-MYC in Burkitt lymphoma; and iv) BCL-6 in diffuse large cell lymphoma (OLOL). The mechanism of chromosomal translocation, the functional consequences of these aberrations on oncogene expression and their role in lymphomagenesis will be reviewed. Emphasis will be on recent findings about the normal and pathological function of the BCL-6 gene, which is expressed in all GO-derived lymphomas and is involved in chromosomal translocations in DLCL. In addition, recent evidence indicates that, although mutations of the promoter region of BCL-6 are found in normal GO B-cells, some mutations found in NHL lead to abnormal BCL-6 regulation in DLCL, follicular lymphoma and Burkitts lymphoma. Finally, novel findings on the molecular dissection of chromosomal abnormalities involving band 1q21, among the most frequent in NHL, will be presented.

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Prognostic factors in mucosa-associated lymphoid tissue lymphomas

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Introduction

Prognostic factors in oncology are developed on the basis of large and preferably uniformly treated patient series in order to predict clinical behavior in terms of overall survival, disease-free survival and reaction to therapy in individual patients. These parameters can be relatively simple clinical parameters, such as age and stage, and can also be tissue-based morphological, immunological and molecular factors. Parameters that may predict prognosis can be related to tumor growth characteristics, to the interaction of the patient with the disease and to the patient's ability to tolerate therapy. Together, these factors serve to guide the choice of therapy. Modern lymphoma classifications are based on the concept of "lymphoma disease-entities". These are characterized by a specific morphological and immunophenotypical spectrum and characteristic molecular alterations in combination with a characteristic clinical presentation and course. Also within well-defined entities, such as mucosa-associated lymphoid tissue (MALT) lymphoma, for example, a spectrum of clinical behavior can be found and parameters to predict this behavior may be identified.

Clinical prognostic factors

The International Prognostic Index (IPI), which was initially developed for diffuse large cell lymphomas, has proven to be of value in many types of lymphoma, including MALT lymphoma. Since the IPI is built up of basic factors that describe the growth characteristics and aggressiveness of the tumor (stage, number of extranodal sites, lactate dehydrogenase) and basic characteristics of patients and their ability to tolerate therapy (age, performance status), this broad applicability in lymphoma may be expected. However, stratification on the basis of these general parameters would ignore the specific characteristics of individual lymphoma disease-entities.