Exp Oncol 2012
34, 4, 377–388

Experimental ONCOLOGY

MATERIALS OF HEMATOLOGY TUTORIAL "DIAGNOSTIC WORK-UP OF HEMATOLOGICAL MALIGNANCIES. FOCUS ON LYMPHOID MALIGNANCIES", MAY 18-19, 2012, KYIV, UKRAINE

For about 20 years, the European School of Hematology (ESH) and the European Hematology Association (EHA) have cooperated in organizing educational activities in the field of continuous medical education designed in collaboration with the international experts. ESH has worked much to improve and harmonize the quality of education in hematology throughout Europe with the active implication of the world's most prominent hematologists and hematology organizations. In 2008, the Joint ESH-EHA Executive Committee was organized. The Committee members E. Gluckman and B. Lowenberg from ESH, W. Fibbe and R. Foa from EHA have developed a framework for continuing collaboration in the field including the workshops and training courses for hematologists. Among the scientific and educational courses on the latest developments in hematology, the hematology tutorials are of great interest for all those who are eager to improve and update their knowledge in various fields of modern hematology.

The scientific program of the tutorials comprising plenary lectures, interactively conducted clinical case study sessions and self-assessment sessions is designed to encourage interaction between the faculty and the course participants. For many years, within the framework of ESH-EHA program for continuous medical education, conferences, training courses and laboratory workshops have been organized in various countries throughout the world. The hematology tutorials involving a faculty of international experts are targeted to clinicians, biologists and students working in the field of hematological malignancies.

It was the first time when the hematology tutorial was held in Kyiv, Ukraine. The 24th Hematology Tutorial promoted a modern view of morphology, pathogenesis, diagnosis and treatment of lymphoid malignancies. The faculty of this tutorial consisted of the leading experts from different countries: Prof. R. Foa and Prof. G. Gaidano from Italy. Prof. C. Dearden from United Kingdom, Prof. S. McCann and Prof. E. Vandenberghe from Ireland, Prof. E. Kimby from Sweden, Prof. D. Gluzman and Prof. I. Kriachok from Ukraine. Among the audience comprising about 200 people were clinicians and researchers specializing in hematology arriving from various cities throughout Ukraine.

As a courtesy of ESH-ESA and personally of the faculty of the meeting, the lecturers have provided their permissions for publishing the extended abstracts of their lectures in this issue of Experimental Oncology.

WHO CLASSIFICATION OF LYMPHOID MALIGNANCIES

D.F. Gluzman
R.E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, National Academy of Sciences of Ukraine
Correspondence: gluzman@onconet.kiev.ua

Lymphoid malignancies are tumors of the immune system that originate from B or T lymphocytes and, rarely, from NK cells. They encompass extremely heterogeneous group of diseases based on their histological forms, biologic and molecular genetic features, sites of clinical presentation (nodal or extranodal), tumor behavior (localized or disseminated), and response to the treatment.

The history of recognition and classification of lymphoid malignancies is long, controversial and complicated. Two classification systems have been widely used until recently, the Kiel classification of non-Hodgkin's lymphomas and the Working Formulation for clinical usage. In 1994 after the immunologic revolution (creation the hybridoma technology that led to the development of monoclonal antibodies) and dramatic progress in understanding the genetics of lymphoid malignancies), the International Lymphoma Study Group (ILSG) of experienced hematologists formulated new proposals for a modern lymphoma classification, the so-called Revised European American Lymphoma (REAL) classification. With some additions and corrections, it has been developed into World Health Organization (2001) classification (E.S. Jaffe, N.L. Harris, H. Stein, J.W. Vardiman, eds. Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues. Lyon: IARC Press, 2001. 351 p.).

The 4th edition of the WHO classification of Tumours of Haematopoietic and Lymphoid Tissues (2008) incorporates new information that has emerged from basic and clinical investigations and includes new defining criteria for some diseases as well as number of new entities defined by a combination of immunophenotype, genetic criteria and clinical features.

The recent WHO classification (2008) has been updated as a joint effort of more than 130 hemopathogists from 22 countries. WHO classification of the B cell, T cell and NK cell neoplasms that in many respects recapitulate normal stage of lymphoid cell differentiation subdividing tumors into those with an immature or blastic appearance versus more mature stage of lymphoid development. This classification system represents a significant advance in our ability to understand, identify and treat different lymphoma entities. It is based on the concept of clinicopathologic entities in which histology, immunophenotype, molecular genetic data as well as clinical features are integrated. The putative cell origin and stage of differentiation of different types of lymphoid malignancies is also taken into account.

According to our experience, the application of immunocytochemical and molecular genetic studies has led to the detection of small number of pathologic cells

in peripheral blood and bone marrow of some patients with non-Hodgkin's lymphomas.

In 1993, the Reference Laboratory was set up as a public service on the basis of the Immunocytochemistry Department of R.E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, National Academy of Sciences of Ukraine with the aim of the precise diagnosis of the haematopoietic malignancies based on cytomorphology, cytochemistry, immunophenotyping and the techniques of molecular biology in accordance with FAB, WHO, EGIL, ICD-10 and ICD-O-2 classifications. The diagnostic activity of the Reference Laboratory covers 35-45% of all Ukrainian patients with acute leukemias, chronic lymphoid and myeloid leukemias, myelodysplastic syndromes, malignant lymphomas, histiocytosis, and metastatic lesions of lymph nodes and bone marrow. At present, the patients with tumors of haematopoietic and lymphoid tissues are diagnosed according to up-to-date WHO classification. We believe that only precise diagnosis of the major types of hematological malignancies to the up-to-date classification with delineation of the specific biological subtypes of hematological malignancies may represent the basis for further molecular biological and epidemiological studies. New insight into the biology of the lymphoid malignancies in the coming years might well improve our ability to evaluate patients and chose therapy.

REFERENCES

1. Ferry YA, Harris NL. Atlas of lymphoid hyperplasia and lymphoma. Philadelphia: W.B. Saunders Co., 1997. 273 p.

2. Human lymphoma: clinical implications of the REAL classification. D.Y. Mason, N.L. Harris (eds.). London etc.: Springer-Verlag, 1999. 554 p.

3. World Health Organization classification of tumours. Pathology and genetics of tumours of haematopoietic and lymphoid tissues. E.S. Jaffe, N.L. Harris, H. Stein, Y.W. Vardiman (eds.). Lyon: IARC Press, 2001. 351 p.

4. Feller AC, Diebold J. Histopathology of nodal and extranodal non-Hodgkin lymphoma. Berlin etc.: Springer-Verlag, 2004. 464 p.

5. The lymphomas, 2nd ed. G.P. Canellos T.A. Lister, B. Young (eds). Philadelphia: Elsevier Inc., 2006. 581 p.

6. WHO classification of tumours of haematopoietic and lymphoid tissues. S.H. Swerdlow, E. Campo, N.L. Harris, E.S. Jaffe, S.A. Pileri, H. Stein, J. Thiele, J.W. Vardiman (eds.). Lyon: IARC Press, 2008. 439 p.

7. Gluzman DF, Sklyarenko LM, Nadgornaya VA. Tumours of haematopoietic and lymphoid tissues (cytomorphology, immunocytochemistry, diagnostic algorithms). Kyiv: DIA, 2008. 193 p. (in Russian)

8. Gluzman DF, Sklyarenko LM, Nadgornaya VA. Diagnostic oncohaematology. Kyiv: DIA, 2011. 256 p. (in Russian).

CHRONIC LYMPHOCYTIC LEUKEMIA

I.A. Kriachok

Oncohematology Department, National Cancer Institute, Kyiv, Ukraine

Correspondence: irina.kryachok@unci.org.ua

Chronic lymphocytic leukemia (CLL) is the most common form of leukemia in Western countries with an incidence of 4.2/100,000/year [1]. The incidence increases to >30/100,000/year at an age of >80 years. The median age at diagnosis is 72 years. About 10% of CLL patients are reported to be younger than 55 years.

The guidelines for the diagnosis and treatment of chronic lymphocytic leukemia were revised by the International Workshop on CLL in 2008 (IWCLL). Criteria for CLL are as follows: the presence in the peripheral blood of 5 x 10^9/L monoclonal B lymphocytes for the at least 3 months. The clonality of the circulating B lymphocytes needs to be confirmed by flow cytometry [2]. Typical immunophenotype of CLL lymphocyte is $CD5^+$, $CD23^+$, $CD43^{+/-}$, $CD10^-$, $CD19^+$, CD20 dim, slgdim$^+$ and cyclin DI^- [3]. Bone marrow examination is not required for diagnosis and a CT scan not required for staging, but flow cytometry is crucial for correct diagnosis.

The first prognostic marker to be used in the clinical management of CLL was the Rai clinical staging system, published in 1975 [4]. This system was later followed by the Binet staging system, published in 1981 [5]. Both of these staging systems provide a basic framework for estimating prognosis and are factored into the current International Workshop on CLL guidelines for initiation of treatment [2].

Multiple factors, measured in standard clinical laboratory tests, affect the clinical course of CLL. These factors include lymphocyte count, lymphocyte doubling time, M level, sTK level, angiopoietin-2 (Ang-2) level, and soluble cluster designation markers (CD14, CD23, and CD49d). Other clinical markers that have been investigated as potential prognostic indicators include age, gender [6], lymphocyte doubling time [7], number of prolymphocytes [8], pattern of bone marrow involvement and percentage of smudge cells [9].

Approximately 80% of individuals with CLL have acquired chromosomal abnormalities within their malignant clone and can be categorized into five prognostic groups accordingly: deletion 13q (median survival, 133 months); deletion 11q (median survival, 79 months); trisomy 12 (median survival, 114 months); normal cytogenetics (median survival, 111 months); and deletion 17p (median survival, 32 months). Reciprocal chromosome translocations are described but are rare in CLL. A complex cytogenetic karyotype can be identified in ~I6% of patients and is commonly associated with poor prognostic features including CD38 expression and unmutated IgHV [10].

The outcome of patients with leukemic cells that use an unmutated IgVH gene is inferior to those patients with leukemic cells that use a mutated IgVH gene. In addition, the VH3.21 gene usage is an unfavorable prognostic marker independent of the IgVH mutational status. Leukemic cell expression of ZAP-70 and CD38 was found to correlate with the expression of unmutated IgVH genes and to predict a poor prognosis.

However, the association between expression of ZAP-70 or CD38 with the expression of unmutated IgVH genes is not absolute. It is uncertain whether leukemia-cell expression of unmutated IgVH genes or ZAP-70 predict the response to treatment or overall survival, once therapy is required. Taken together, further clinical trials are needed to standardize the assessment of these pa-