

# session 11 – special topic: classifying lymphoma

## 112 THE WORLD HEALTH ORGANIZATION (WHO) CLASSIFICATION OF LYMPHOID NEOPLASMS: WHAT'S NEW?

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The World Health Organization (WHO) Classification of Tumors of the Hematopoietic and Lymphoid Tissues (3rd ed) was published in 2001. It was based on the principles of the Revised European-American Classification of Lymphoid Neoplasms (REAL), published in 1994 by the International Lymphoma Study Group (ILSG). It is a list of “real” disease entities, which are defined by a combination of morphology, immunophenotype, genetic features, and clinical features. The relative importance of each of these features varies among diseases, and there is no one “gold standard.” In 2006, the process of revising the classification for the 4th edition of the series began. The Society for Hematopathology and the European Association of Hematopathologists appointed a steering committee to conduct the revision. Over 75 international hematopathologists and a similar number of hematologists and oncologists were involved in revising the classification and writing the 4th edition of the book. Two Clinical Advisory Committee (CAC) meetings were held, one for myeloid neoplasms and acute leukemias and one for lymphoid and histiocytic neoplasms. Recently recognized genetically-defined entities were added to the classification of myeloid neoplasms. Consensus criteria developed by international groups for the diagnosis and staging of entities such as CLL, Waldenström's macroglobulinemia, plasma cell myeloma, and cutaneous lymphomas were included. New entities within the category of DLBCL were recognized. Distinctive variants of follicular lymphoma (FL) and nodal marginal zone lymphoma common in the pediatric age group were recognized, as well as EBV + DLBCL, more common in the elderly. Anaplastic large-cell lymphoma ALK+ was recognized as an entity, distinct from ALK- cases. Categories were created for cases that are borderline between DLBCL and BL and between classical HL and DLBCL. Grading of follicular lymphoma remains controversial. The role of biomarkers and microarray expression profiling studies in the classification remains to be determined.

## 113 PERIPHERAL T-CELL LYMPHOMA, NOT OTHERWISE SPECIFIED: A CLINICOPATHOLOGIC STUDY OF 340 CASES FROM THE INTERNATIONAL PERIPHERAL T-CELL LYMPHOMA PROJECT

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**Introduction:** Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS), is an uncommon lymphoma in which the clinical and pathological features of prognostic importance are not well understood.

**Methods:** We collected 340 cases of PTCL-NOS from 22 centers in 13 countries around the world. All patients were >19 years old and initially presented between January 1, 1990, and December 31, 2002. A panel of immunostains was performed and a consensus diagnosis was reached by a panel of expert hematopathologists in each

case. Survival outcomes were evaluated according to various clinical and pathological features.

**Results:** PTCL-NOS was the most common subtype of PTCL in the project (29.3%) and consisted mainly of PTCL unspecified (88.5%) and the lymphoepithelioid type (8.2%). The median age of the patients was 60 years, 66% were males, and 69% had stage III/IV disease at diagnosis. Anthracycline-based chemotherapy was given to 80% and a complete response was obtained in 56% of the patients. However, the 5-year overall and failure-free survivals for the entire group were only 32% and 20%, respectively. The International Prognostic Index (IPI) was highly predictive of survival ( $p < 0.001$ ). Other clinical prognostic factors identified in multivariate analysis (MVA) included hypergammaglobulinemia (HR 0.5), mass >10 cm (HR 2.5), and platelets <150,000/mm<sup>3</sup> (HR 2.2). Pathological features predictive of survival included >70% transformed cells (HR 1.7) and <10% CD8+ background T-cells (HR 1.8). In situ stains for Epstein-Barr virus (EBERs) revealed that a heavy viral load predicted for poor survival in young patients (<60 years), but not older patients. However, in final MVA, only the IPI and >70% transformed cells were predictive of survival.

**Conclusion:** PTCL-NOS is an aggressive disease in which the IPI and the percentage of transformed cells could be used to select patients for risk-adapted therapies.

## 114 ANGIOIMMUNOBLASTIC T-CELL LYMPHOMA: A REPORT FROM THE INTERNATIONAL PERIPHERAL T-CELL LYMPHOMA PROJECT

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The International Peripheral T-cell lymphoma (PTCL) Project was undertaken to study these lymphomas and compare them in North America, Asia and Europe. Consecutive, well-documented cases of PTCL were classified by a panel of expert hematopathologists and clinical and pathological features were correlated with survival. 243 cases of angioimmunoblastic T-cell lymphoma (AILT) were diagnosed (21% of all PTCLs). Pathologist's agreement was 81% in their diagnosis. AILT occurred most frequently in Europe (28%) compared to Asia (17%) and North America (15%). At presentation, generalized lymphadenopathy was noted in 76% of the patients. Hemolytic anemia was seen in 13% and dysproteinemia occurred in 50%, a monoclonal serum immunoglobulin was seen in 8% of the patients. Anemia, hypergammaglobulinemia and elevated LDH were more frequent in AILT than in PTCL-unspecified. Patients with AILT had a significantly higher frequency of advanced stage disease (89% of the patients were stage 3 or 4), as well as worse prognostic factors. Stage did not influence survival. The 5-year overall (33%) and failure-free survival (18%) of patients with AILT was similar to those with PTCL-unspecified. Treatment was usually administered in combination with an anthracycline, but their administration did not influence survival. A few factors at presentation were prognostic for outcome, including the PIT (prognostic index for T-cell lymphoma), age, B-symptoms and performance status. The IPI was not prognostic.

In conclusion, AILT is an aggressive disease for which new treatments are clearly needed. Clinical features such as the PIT, B-symptoms and platelet count could be used to select patients for risk-adapted strategies.