

574 ESTABLISHMENT AND CHARACTERISATION OF AN ALK-POSITIVE DIFFUSE LARGE B-CELL LYMPHOMA CELL LINE WITH T(2;17) LEADING TO CLTC-ALK FUSION

C. Damm-Welk¹, W. Klapper², I. Nielaender³, L. Harder³, R. Siebert³, W. Woessmann¹

¹Pediatric Hematology and Oncology, Justus-Liebig-University, Giessen, Germany, ²Pathology, Christian-Albrechts-University, Kiel, Germany, ³Human Genetics, Christian-Albrechts-University, Kiel, Germany

Anaplastic lymphoma kinase (ALK)-positive diffuse large B cell lymphoma (DLBCL) with expression of CD38 and lack of CD30 was first described in 1997. With few exceptions these ALK-positive DLBCL show a fine granular cytoplasmic ALK-staining characteristic for the fusion of CLTC with ALK caused by the reciprocal translocation t(2;17)(p23;q23). This rare but characteristic lymphoma subtype is associated with a poor outcome. We here report the establishment and characterisation of the first ALK-positive DLBCL cell line, called LM1. LM1 was derived from the bone marrow of a 13 year-old girl suffering from a systemic relapse of an ALK-positive DLBCL. The relapse occurred early after allogeneic bone marrow transplantation for progression during first line therapy. The immunophenotype of the LM1 cells was confirmed to be identical to that of the primary tumor. LM1 cells express CD138, VS38c, CD38 and EMA. The cells show fine granular cytoplasmic ALK-staining and expression of the immunoglobulin kappa light chain as well as gamma heavy chain. Negativity for CD30, T cell markers and CD20 and CD79a further confirmed the diagnosis.

The tumor cells carry a complex near tetraploid karyotype described as: 74~91<4n>.XXXX,del(1)(p10p35),t(2;17)(p23;q23)x2,add(2)(p11),der(4)t(4;15)(p14;q15),add(7)(q34~q35)x2,der(9)t(9;13)(q24;q12)x2,add(17)(p11)x2,inc[cp15]. Multicolour FISH with probes for the ALK and CLTC loci confirmed presence of the translocation t(2;17)(p23;q23) and CLTC-ALK fusion. The expression of the CLTC-ALK fusion transcript could be demonstrated by RT-PCR with specific primers followed by sequencing in both the primary tumor and LM1 cells. Immunoblot analysis with an ALK antibody showed an exclusive cytoplasmically expressed protein of the expected molecular weight for CLTC-ALK. The cell line provides opportunities to further study the cell of origin, pathogenesis and causes of chemoresistance of this rare lymphoma subtype.

575 CLINICAL CHARACTERISTICS AND OUTCOME OF DIFFUSE LARGE B-CELL LYMPHOMA IN ADOLESCENTS AND YOUNG ADULTS: A SINGLE CENTER EXPERIENCE ON 49 PATIENTS

M. Ebbo², D. Coso², V. Ivanov², J. Rey², B. Chetaille³, A. Stoppa², J. Schiano², T. Aurrant², R. Bouabdallah¹

¹Dpt of Hematology, Lymphoma Unit, Institut Paoli-Calmettes, Marseille, France, ²Hematology, Institut Paoli-Calmettes, Marseille, France, ³Pathology, Institut Paoli-Calmettes, Marseille, France

Introduction/Background: Because aggressive lymphoma is a disease which mainly concerns population with a median age at 58 years to 60 years, we conducted a retrospective analysis in adolescents and young adults with diffuse large B-cell lymphoma (B-DLCL), in order to describe their clinical characteristics and outcome after treatment.

Patients and Methods: The lymphoma data base collection was analyzed from 1995 to 2006. The patients had to be less than 30 years, with a B-DLCL. Depending on the time of diagnosis, patients received chemotherapy with or without rituximab, and autologous stem cell transplantation (ASCT) was delivered as first line treatment in poor prognosis patients.

Results: 570 patients with B-DLCL were recorded in our data base, of whom 49 (9%) were <30 years. The median age was 26 years (range 15 to 29), and sex ratio at 1. Performance status was normal in 71% of patients, whereas lactate dehydrogenase level was increased in 60% of patients. The disease was disseminated in 71% of patients, 18% had a bone marrow involvement, and 79% of patients presented with a bulky disease. The Age-adjusted International Prognostic Index score was ≥ 2 in 60% of patients. Twenty-eight patients (57%) received a rituximab containing regimen, and 32 (65%) underwent ASCT as consolidation treatment. The complete response rate was 75%. With a median follow-up of 60 months, the 5-year overall survival (OS) and event-free survival (EFS) rates (mean +/- SD) were 66% +/- 14% and 57% +/- 14%, respectively. Bulky disease did not influence outcome of patients ($P=0.9$), and the addition of rituximab to chemotherapy regimen showed no statistical difference either in OS ($P=0.3$) or EFS ($P=0.5$).

Conclusion: B-DLCL in adolescents and young adults is an aggressive disease that often presents with adverse prognostic factors. However, when treatment is adapted to

the disease risk, outcome is equivalent to that observed in patients under 60 years with B-DLCL.

576 LYMPHOBLASTIC LYMPHOMA: DIAGNOSIS, TREATMENT AND PROGNOSIS (ABOUT 19 CASES)

R. Ben Amor¹, H. Ben Mechlia¹, R. Jeddi¹, L. Aissaoui¹, R. Ben Lakhal¹, K. Kacem¹, H. Ben Abid¹, Z. Belhadjali¹, B. Meddeb¹

¹Hematology, Aziza Othmana Hospital, Tunis, Tunisia

The aim of this study is to revise the clinical profile and to evaluate the prognostic and the therapeutic results of patients with lymphoblastic lymphoma (LL). We present a retrospective study of 19 cases of LL treated in the department of Haematology at the Aziza Othmana Hospital of Tunis. In our study the rate of LL is estimated at about 10% of Non Hodgkin Lymphomas (NHL) diagnosed at the same period (192). Median follow-up was 30 months (6-131). All our patients had histologic and immunophenotypic documentation. The median age at diagnosis was 21 years (age range 6-43). Nine patients (47%) were children (<17 years) and ten (53%) were adults. Patients with bone marrow localisation ($\geq 20\%$), considered as acute lymphoblastic leukaemia (ALL), were not included. Sex ratio was 2,1 (13 males and 6 females). Diagnosis was performed by: discovery of peripheral nodes in 47%, worse performance statue (>2) in 42%, dyspnoea in 47% and a superior vena cava syndrome in 31% of cases. Localizations were exclusively nodal in 31% (6). At diagnosis 74% were T-cell immunophenotype, 84% were stage III to IV. 60% had mediastinal involvement, 45% had a pleural/pulmonary involvement and 10% had central nervous system (CNS) disease. The other localizations were: pericardia effusion (20%), liver (10%), bone marrow (5%), and bone (5%). All patients younger than 20 years old (57%) received ALL children chemotherapy protocol (EORTC). Eight adults (43%) received an intensive ALL designed chemotherapy regimen inspired from children's protocols. Autologous stem cell transplantation was performed in only one partial remission case. Overall, 10 patients (53%) achieved a complete remission (CR), 5 patients (26%) achieved a partial remission, and 4 patients (21%) died during induction. Five patients (26%) relapsed within 12 months. The estimates of overall survival (OS) and the event free survival (EFS) at 3 years are respectively at 63% and 52%. No parameters (stage, serum lactate dehydrogenase [LDH], sex) appeared to influence outcome except children's disease which had a better issue. In fact the children CR, OS and EFS compared with adults were respectively at 80% vs 30%, 80% vs 50% and 66% vs 40%. Finally, we note that in our study the rate of LL (10% of all NHL) is higher than reported studies (4%) and more aggressive in adults.

577 OUTCOME OF TREATMENT IN CHILDREN WITH B-NON-HODGKIN'S LYMPHOMA AND B-ACUTE LYMPHATIC LEUKEMIA

M. Aničić¹

¹Hematology and Oncology Dept., Children's Clinic Salata, Zagreb, Croatia

Purpose: The aim of the study was to evaluate the therapeutic efficacy of BFM-NHL chemotherapy protocol alone and in combination with monoclonal antibodies (Rituximab).

Patients and methods: During the 1990-2007 period, 31 children with B-NHL (17 male and 14 female) and 3 with B-acute lymphatic leukemia (2 male and 1 female), aged 2-16 (mean age 9.6) years, were treated according to the NHL-BFM protocol. Therapy consisted of 5-day pretreatment (standard chemotherapy dosage) combined with 2-6 cycles of high-dose chemotherapy; in addition, ten patients (with CD 20 antigen) received monoclonal antibodies (Rituximab) and 2-6 cycles of high-dose chemotherapy in 2006 and 2007. Patients were divided into three risk groups.

Results: Complete remission was achieved in all 34 (100%) patients; disease relapse and lethal outcome were recorded in three (9%) patients; in 31 (91%) patients, the first complete remission has been persisting to the present. Grade III and IV toxicity was mostly observed after the first and second cycle of chemotherapy; patients treated with monoclonal antibodies (Rituximab) and high-dose chemotherapy had less severe side effects. Rituximab was well tolerated and no major side effect was encountered. In one patient, secondary tumor disease (AML) developed 4 years of treatment discontinuation.

Conclusion: Therapeutic results were very good and consistent with those reported from other European centers. It seems that combined modality therapy using monoclonal antibodies (Rituximab) and chemotherapy is optimal treatment for children with B - non-Hodgkin's lymphoma (CD 20 +) and B- acute lymphatic leukemia (CD 20 +). Careful evaluation and large prospective studies are needed to verify real impact on patient management.