T-cell lymphoma

504 THE CLINICAL SPECTRUM OF LARGE GRANULAR LYMPHOCYTIC LEUKAEMIA: A CASE SERIES
K. Kelly1, A. Fortune1, J. Sargent2, F. Quinn1, K. Haslam1, D. O’Brien1, E. Conneally3, P. Browne1, P. Thornton1, E. Vanderzande1
1Haematology, St James Hospital, Dublin, Ireland, Republic of, 2Haematology, Mater Hospital, Dublin, Ireland, Republic of, 3Department of Lymphoma, Singapore General Hospital, Singapore, Singapore

#co first author

Large Granular Lymphocytic Leukemia (LGL) is an indolent T lymphoproliferative disorder. Molecular analysis of the T cell receptor (TCR) gene to define clonal T populations has made LGL diagnosis robust and clarified its natural history. We confirm the indolent presentation but highlight the ultimate requirement for therapy.

Fifteen patients, aged between 44 and 78 were referred to haematology by their general practitioner with non-specific symptoms of fatigue (53%), recurrent infections (40%) and minor blood count abnormalities. The median time from symptom onset to diagnosis was 7 months. Eleven (73%) patients were neutropenic and 3 had an absolute lymphocytosis (>5 x 10⁶/L). An excess of LGL and abnormal immunophenotype pattern was noted: CD5+, CD7 weak, CD4–CD8 ratio reversal and CD56+. Clonality was confirmed using TCRβ Y and 6 biomed probes, of which 7 had β9 Y and 5 δ gene rearrangements.

Ten (67%) patients needed treatment for a symptom or a neutrophil count <0.5 x 10⁹/L. Of these, 4 patients received cytosporine as first line therapy, resulting in a temporary improvement in blood count in 3 patients. Moteserate and Chlorambucil were used in 4 patients with no improvement.

Six patients received Pentostatin, either first line (3 cases) or after 2 cycles of therapy, resulting in a complete haematological response in three patients (including 1 molecular remission) and a partial haematological response in a further 2 patients. Two patients relapsed 18 months after Pentostatin, with 1 patient achieving a further remission with alemtuzumab and the second patient with a 20-year history of LGL and many lines of treatment proceeding to allogeneic bone marrow transplantation.

LGL leukemia is probably under-diagnosed resulting in non-specific morbidity in the community. Accurate diagnosis using molecular techniques is now possible. In our hands Pentostatin has been an effective, well-tolerated treatment for symptomatic LGL. Clarity on indications for treatment and a logical treatment algorithm might improve the morbidity of this disease.

505 STAGE AND AGE ARE THE MAIN PROGNOSTIC FACTORS IN PATIENTS WITH NASAL-TYPE NATURAL KILLER (NK)/T-CELL LYMPHOMA OF THE UPPER AERO Digestive TRACT
J.W. Tham1, Y.P. Yap1, S. Hee2, L. Lim3, R. Quek1, G. Lim1, L. Tan1, S. Ng1, M. Tao1, S. Loong1
1Department of Radiation Oncology, National Cancer Centre, Singapore, Singapore, 2Department of Medical Oncology, National Cancer Centre, Singapore, Singapore, 3Department of Hematology, Singapore General Hospital, Singapore, Singapore, 4Department of Pathology, Singapore General Hospital, Singapore, Singapore

Introduction: We reviewed the clinical features, treatment and outcome of this disease seen between 1996 and 2007.

Material and methods: Case records of 44 patients were retrospectively reviewed.

Results: Median age was 50. Twenty-four (55%) were stage I, 11 (25%) were stage II, 2 (5%) were stage III and 7 (16%) were stage IV. Median follow-up was 36 months for patients alive at time of censorship. 27 patients had both chemotherapy (CT) and radiotherapy (RT); 10 had RT alone; 5 had CT alone and 2 were treated symptomatically only. 27 (61%) had complete response to treatment, 2 (5%) had partial response, 8 (18%) had progressive disease and 7 (16%) deteriorated so rapidly that response was not evaluable. Of the complete responders, 3 recurred at locoregional sites, 5 at distant sites and 3 at both. 21 (48%) deaths were recorded in total, all within 2 years of diagnosis. 3-year disease free survival (DFS) was 36%; 5-year overall survival (OS) was 51%. Univariate analysis showed that good performance status (ECOG 0-1), absent or with a median time from diagnosis to treatment of 11 months. Five patients achieved CR or PR, they received AH SCT combined with high dose radiotherapy/chemotherapy. Eighteen of them received autologous peripheral blood stem cell transplantation (APR SCT), and the left received autologous bone marrow transplantation (ABMT).

Conclusion: The patients with nasal NK/T cell lymphoma achieved CR or PR after induction therapy, followed by HDCA/ABMT. AH SCT combined with high dose radiotherapy/chemotherapy is an effective treatment for patients with poor prognostic nasal NK/T cell lymphoma.

506 TREATMENT OUTCOME AND PROGNOSIS ANALYSIS OF AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPANTATION COMBINED WITH HIGH DOSE RADIOTHERAPY/ CHEMOTHERAPY IN 22 CHINESE PATIENTS WITH NASAL NK/T CELL LYMPHOMA
X. Qiu1, H. Wang1, X. Liu1, H. Zhang1, W. Li1, M. Wang1
1Department of Lymphoma, Tianjin Medical University Cancer Hospital, Key Laboratory of Cancer Prevention and Therapy, Tianjin, China

Introduction: To analyze the outcome and prognosis of autologous hematopoietic stem cell transplantation (AH SCT) combined with high dose radiotherapy/chemotherapy in 22 patients with nasal NK/T cell lymphoma.

Material and methods: From July 1992 to December 2005, 22 patients with nasal NK/T cell lymphoma were diagnosed pathologically. According to Ann Arbor staging classification, 1 patient was stage IA, 9 IE, 4 IIIE and 8 IV. Of 22 patients, 10 patients had IPI of 1–2, the left had IPI of 3–4. 16 patients had B symptom. 10 patients achieved a complete remission (CR), 12 patients achieved a partial remission (PR) after receiving chemoradiotherapy or chemotherapy combined with radiotherapy. When the patients achieved CR or PR, they received AH SCT combined with high dose radiotherapy/chemotherapy. Eighteen of them received autologous peripheral blood stem cell transplantation (APR SCT), and the left received autologous bone-marrow transplantation (ABMT).

Results: Median follow-up duration was 76 (24–180) months. The 5-year and 8-year overall survival (OS) was 79.3% and 64.1%, respectively. The 5-year and 8-year disease free survival (DFS) was 57.4% and 50.2%, respectively. The 5-year OS for Stage I–II disease and III–IV disease was 90.0% and 70.8%, respectively (P=0.041). The 5-year OS for patients without and with B symptom were 100.0% and 70.7%, respectively (P=0.045). The 5-year OS for IPI 1–2 and 3–4 were 100.0% and 60.0%, respectively (P=0.009). On multivariate analysis by COX regression, disease stage B symptom and IPI were found to be significant prognostic factors.

Conclusion: The patients with nasal NK/T cell lymphoma achieved CR or PR after induction therapy, followed by HDCA/ABMT. AH SCT combined with high dose radiotherapy/chemotherapy is an effective treatment for patients with poor prognostic nasal NK/T cell lymphoma.

507 PROGNOSTIC ANALYSIS OF 61 CASES OF NASAL NK/T CELL LYMPHOMA
Z. Song1, H. Wang1, X. Qiu1
1Department of Lymphoma, Tianjin Medical University Cancer Hospital, Key Laboratory of Cancer Prevention and Therapy, Tianjin, China

Introduction: To investigate the clinical features and prognostic factors of extranodal nasal NK/T cell lymphoma (ENKTL).

Material and methods: Records of 61 patients with pathologically confirmed ENKTL were reviewed. Detailed clinical and laboratory data were included in univariate analysis, and statistically significant factors in univariate analysis were then included in multivariate analysis.

Results: In univariate analysis Ann Arbor stage performance status (IP), number of extra-nodal site, B symptoms, LDH and β2-MG level were found to be the prognostic factors associated with time to overall survival in ENKTL. In multivariate analysis, Ann Arbor stage performance status LDH and β2-MG level were independent prognostic factors of overall survival.

Conclusion: Ann Arbor stage performance status LDH and β2-MG level were demonstrated as independent prognostic factors of the overall survival in ENKTL.

508 L-ASPARAGINASE IN THE TREATMENT OF EXTRANODAL NK/T-CELL LYMPHOMA NASAL-TYPE
W. Yong1, W. Zheng1, J. Zhu1
1Medical Oncology, Beijing Cancer Hospital, School of Oncology, Peking University, Beijing, China

Background: Extranodal NK/T-cell lymphoma (NK/TCL), nasal-type pursues aggressive clinical course with poor prognosis, and for this condition there is no optimal therapy. The purpose of this study was to investigate treatment outcome of chemoradiotherapy including L-asparaginase-based regimen.
Patients and methods: Fifty-two patients with extranodal NK/TCL, nasal-type were enrolled. Two cycles of CHOP regimen were given as initial chemotherapy. The patients sensitive to CHOP regimen received CHOP chemotherapy followed by primary involved-field radiation (IF RT) (CHOP-sensitive group). The patients resistant to CHOP regimen were altered to receive L-asparaginase-based salvage regimen plus primary IF RT (L-asparaginase group).

Results: Forty patients had stage I-II disease. Twelve patients had stage III-IV disease. Nasal cavity was the most primary organ in 41 patients but extra-upper aerodigestive tract only in 4 patients. Fourteen patients were sensitive to initial CHOP regimen and reached CR after CHOP chemotherapy plus RT. Thirty-seven patients resistant to CHOP chemotherapy received L-asparaginase-based chemotherapy plus RT except that one patient died during first cycle of CHOP chemotherapy, and 59.5% (23/37 patients) achieved CR. The CR rate for the whole group was 69.2% (37/52 patients). The 5-year overall survival (OS) rates were 68.2% for the whole Group and 66.6% for L-asparaginase plus RT group. On univariate analysis, disease stage, fever symptom and performance status were significant factors for OS. On multivariate analysis, only disease stage was an independent factor influencing OS. Fourteen patients had died. Six patients died from systemic progression, one patient from intestinal perforation, four patients from massive bleeding of tumor tissue, three patients from hemophagocytic syndrome (HPS).

Conclusion: L-asparaginase regimens combined with primary IF RT may be a useful treatment option and may improve the treatment outcome for NK/TCL, nasal type.

500 CLINICOPATHOLOGICAL FEATURES AND OPTIMAL TREATMENT STRATEGIES FOR ALCL PATIENTS

H. Xiaolu1, L. B1, Z. Shuangmei1, X. Lijian1, S. Yuxiao1
1Department of Medical Oncology, Cancer Institute and Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (CAMS & PUMC), Beijing, China

Introduction/background: Anaplastic large-cell lymphoma (ALCL) is a distinct entity of non-Hodgkin lymphoma. By far, no standard chemotherapy regimen has been established for systematic ALCL patients. To investigate the clinicopathological features of anaplastic large-cell lymphoma and explore the optimal treatment strategies, clinical data of 64 patients were analyzed retrospectively.

Materials and Methods: Sixty-four primary systematic ALCL patients who were diagnosed and treated in our hospital were studied retrospectively.

Results: Our data confirmed the male predominance, young age of onset and frequent presence of adverse factors such as B symptoms and involvement of extranodal sites in ALCL patients. However, patients with stage III-IV disease and elevated LDH were less frequent in our study. Chemotherapy including CHOP and proMACG/ cytBOM was administered in 46 and 9 patients, respectively. No significant difference can be seen in terms of response rate and survival between these two groups. Altogether, 16 patients received peripheral blood stem cell transplantation (PBSC). Although significantly higher proportion of patients in transplantation group had state III/IV disease, the long-term survival was comparable with that of patients received conventional chemotherapy. Anaplastic lymphoma kinase (ALK) was an independent prognostic factor, especially for adult ALCL patients, whose expression indicated significantly high long-term survival.

Conclusions: CHOP is still the first-line chemotherapy regimen for ALCL patients due to its less toxicity and comparable efficacy with third-generation regimen. Patients with advanced disease may potentially benefit from PBSC.

510 PROGNOSTIC FACTORS IN PATIENTS WITH T-CELL NON-HODGKIN LYMPHOMA

L. Casanasana1, C. Flores1, C. Saranne2, C. Barrionuevo1, J. Leon1
1Medical Oncology Department, Instituto Nacional de Enfermedades Neoplasicas, Lima, Peru

Background: Non-Hodgkin Lymphoma (NHL) is a malignant neoplasm of lymphoid system with marked differences in presentation and prognosis. T-cell Non-Hodgkin Lymphoma (T-NHL) represents in our country an important percentage and is generally more aggressive with poorer prognosis than B-cell lymphoma. The objective was to determine the prognostic factors in patients with T-NHL.

Methods: 378 clinical records of patients with T-NHL diagnosed at IDEN between 1998 and 2002, were reviewed. We described the clinicopathological, treatment, response and survival. The survival curves were estimated by Kaplan-Meier and compared by Logrank or Breslow test. The prognostic factors for disease-free survival (DFS) and overall survival (OS) were identified by Cox model.

Results: The median age was 45 years (range: 14-99) and 60% were male. The clinical characteristics were: Zubrod 2 (54%), primary node disease (62%), secondary stage III-IV (58%), B-symptoms (36%), anemia (43%), leukocytosis (30%), increased DHL and B2M in 79% and 49% respectively. According to REAL classification the most frequent histologic subgroup were PTCL unspecified (38%), ATL (24%) and ALCL (17%). 303 (80%) patient received treatment: chemotherapy (CT) 73%, radiotherapy (RT) 11% and CT+RT 15%; CHOP was the most frequent CT scheme (92%). Of 221 patients with CT, 55 (29%) had complete response (CR) and 27 (12%) partial response (PR); 23/55 (42%) patients with CR had recurrence. The 5-year DFS and OS were 39% and 24%. The prognostic factors for OS were Zubrod ≤2 (p=0.007, RR: 16), B symptoms (p<0.001, RR: 1.9) and increased DHL (p=0.007, RR: 1.9). The clinical features were not prognostic factors for DFS.

Conclusions: The presentation of T-NHL was similar to other series, although with higher frequency of anaemia and increased DHL. DFS and OS were similar to other series. Increased DHL is prognostic factor to take into consideration in the follow-up. The clinical stage III-IV is not a prognostic factor in T-NHL.

511 CLINICOPATHOLOGIC AND IMMUNOPHENOTYPIC CORRELATIONS IN 7 CASES OF ENTEROPATHY-TYPE T-CELL LYMPHOMA

C. Panizo1, A. Panizo2, M. Perez-Salazar3, E. Zoazaya1, J. Martinez-Penuela2, J. Parodi2
1Hematology, University Clinic of Navarra, Pamplona, Spain; 2Pathology, University Clinic of Navarra, Pamplona, Spain; 3Pathology, Hospital Reina Sofia, Turtleso, Spain

Background: Enteropathy-type T-cell lymphoma (ETCL) is a rare tumor of intraepithelial lymphocytes occurring in adults with a background of coeliac disease (CD). ETCL is often disseminated at diagnosis, and extrasternal presentations are not uncommon. We studied ETCL features in 7 patients.

Results: There were 5 men and 2 women with a mean age of 54.7 years. All patients had a documented clinical history of adult-onset CD unresponsive to gluten-free diet. Presenting symptoms were abdominal pain, small-bowel perforation or B symptoms. One patient had an extraintestinal presentation of the lymphoma (malignant sinus). Histology of the tumor showed pleomorphic large cells, with vesicular nuclei, prominent nucleoli, and abundant cytoplasm. Intracytoplasmic spread of an epitheliotrophic T-cell population was observed even at distant segments of the small bowel. All cases were CD50+, and showed evidence of T-cell lineage with cytotoxic potential by expression of cytotoxiclastic CD3, CD43, or CD45RO; or perforin; and EMA was performed in tumors and adjacent intestinal mucosa.

Conclusions: ETCL is an aggressive and fatal complication of CD. Gluten-free diet failure may indicate progression to ETCL. Phenotype (cytotoxiclastic CD3+, CD8+, CD50+) and intrapathelial accumulation of lymphoma cells in the adjacent surviving mucosa is clues to the diagnosis.

512 VINORELBINE/GEMCYTABINE IS A SAFE AND ACTIVE COMBINATION IN REFRACTORY CUTANEOUS T-CELL LYMPHOMAS

D.J. Joske1, G. Cull1, B. Augustson2, S. Hyde1, B. McLeod1, M. Bell1
1Haematology Department, Sir Charles Gairdner Hospital, Perth, Australia

Introduction: The treatment of cutaneous T-cell lymphomas remains problematic. Active systemic therapies are needed and the role of stem cell transplantation is not clearly defined. CHOP, for example gives poor results. We treated a small cohort of patients with a novel regimen that was well tolerated and appears capable of providing durable remission in pre-treated patients with advanced stage disease.

Methods: Sequential patients with cutaneous T-cell lymphomas who had failed one or more prior systemic therapies were treated with vinorelbine 30 mg/m² and gemcitabine 1000 mg/m² days 1 and 8, q21 (“vin-gem”), for four cycles. In suitable patients, this was followed by BEAM conditioning and autologous peripheral blood stem cell transplantation. Patients underwent systemic staging and medical photography to record progress.

Results: Five patients with mycosis fungoides (n=4) and cutaneous peripheral T-cell lymphoma (n=1) were included. There were 4 males and 1 female with ages of 45, 58, 65, 70 and 70 years. All had been treated with topical therapy including PUVA, steroids, UVB, and light therapy. Other early therapies included oral azathioprine (n=1), oral methotrexate (n=1) and dapsone (n=1). Prior systemic therapies included CHOP ICE, Arm B HyperCVAD (all in the one case) and desipirtex (n=4; average 11 cycles, range 2–3). A clinical decision to treat with vin-gem was made. Vin-gem caused mild myelosuppression and minimal toxicity; there were no in-patient admissions for sepsis. In the three younger patients, after four vin-gem cycles, BEAM conditioning and autologous peripheral blood stem cell transplantation. Patients underwent systemic staging and medical photography to record progress.

Conclusions: ETCL is an aggressive and fatal complication of CD. Gluten-free diet failure may indicate progression to ETCL. Phenotype (cytotoxiclastic CD3+, CD8+, CD50+) and intrapathelial accumulation of lymphoma cells in the adjacent surviving mucosa is clues to the diagnosis.

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513 DEFUCOSYLATED HUMANIZED ANTI-CCR4 MAB KW-0761 AS A NOVEL IMMUNOTHERAPEUTIC AGENT FOR PERIPHERAL T-CELL LYMPHOMA

T. Ishiia1, T. Ishii2, A. Utsunomiyaa1, A. Inagakia1, H. Yano1, H. Kornuts1, S. Ikeda1, K. Nakanuraa, M. Iwasae1, K. Shitarata2, R. Ueda3
1Department of Internal Medicine, Nippon Medical School, Tokyo, Japan, 2Department of Pathology, Kanagawa Prefectural Seiroku Medical Center, Kanagawa, Japan, 3Department of Clinical Chemistry, Kanagawa Prefectural Seiroku Medical Center, Kanagawa, Japan

Introduction: Peripheral T-cell lymphomas (PTCL) have poor prognosis. The binding kinetics of anti-CCR4 mAbs to CCR4-derived peptide was measured using the BiACore system. ADCC was determined by standard 4-h 51Cr release assay. In vivo antitumor activity of KW-0761 was examined using SCID mouse xenograft models.

Results: The binding affinity of KW-0761 to CCR4 was almost the identical to KM2760 and humanized (KW-0761) anti-CCR4 mAbs. Previously we reported that ADCC with KM2760 was enhanced, making it a promising new agent for treating CCR4-positive lymphoma. Here, we assess the therapeutic potential of the humanized version of this antibody against CCR4-positive T-cell lymphoma.

Materials and Methods: The binding kinetics of anti-CCR4 mAbs to CCR4-derived peptide was measured using the BiAcore system. ADCC was determined by standard 4-h 51Cr release assay. In vivo antitumor activity of KW-0761 was examined using SCID mouse xenograft models.

Conclusions: KW-0761 could be a promising therapeutic agent for patients with CCR4-positive T-cell lymphomas. The efficacy of KW-0761 is being investigated in a clinical trial which we are currently conducting in Japan (ClinicalTrials.gov: NCT00555472).

514 TREATMENT OF PERIPHERAL T-CELL LYMPHOMAS – SINGLE CENTRE EXPERIENCE

K. Pukavics1, Z. Borbély1, I. Martoni1, A. Szikra1, E. Bagai2, L. Krenacs2
1Department of Internal Medicine, Abertawe Beaufort Hospital, Swansea, United Kingdom, 2Department of Pathology, University of South Wales, Pontypridd, Wales, UK

Introduction: Peripheral T-cell lymphomas (PTCL) are a rare type of non-Hodgkin lymphoma (NHL) and represent 15-20% of aggressive NHL cases. PTCLs more frequently involve extranodal site compared to B-cell lymphomas, and have a worse prognosis.

Patients and methods: The authors evaluated 30 patients with PTCL (male/female ratio was 13/17) treated between 2000 and 2005. All the patients classified according to WHO classification criteria. The median age of patients was 59.5 years. The median follow-up time was 13.5 months.

Results: Twenty-seven of the 30 patients were treated with chemotherapy alone (23/CHOP, 3/MegaCEOP, 4/ProMACE-CytaBOM) and 3 with chemotherapy and immunotherapy. Fourteen patients achieved complete remission (CR), 9 had partial remission, 7 were non-responders. Out of the 14 CR patients, 5 were alive, continuously CR. Three patients out of the CR patients underwent autologous stem cell transplantation in the first remission (1 alive, 2 died of progressive disease). Out of the CR patients, after the first chemotherapy 9 relapsed, the 9 patients with partial remission and the 7 non-responders showed continuously progressive disease despite the treatment. They could not achieve second remission with salvage therapy, and died of progression.

Conclusion: Conclusion: The prognosis of PTCL is poor. The new treatment strategies need to be developed in order to achieve better response and long term remission.

515 A CLINICAL STUDY IN PERIPHERAL T NON HODGKIN LYMPHOMA

V. Klyaz1, M. Tsigovici2, T. Kamiriri1, M. Bakiri1, S. Delimpas1, I. Apostolidis1, S. Gigantes1, M. Pagoni1, I. Baltadaiki1, D. Karakasis1, N. Harhalaki1, E. Nikiolaki1
1Haematology Department, Evangelismos Hospital, Athens, Greece

Introduction: Peripheral T-NHL (PTL), comprise a variety of disease entities, which result from post-thymic T lymphocytes, according to morphology, immunophenotype and histopathology. The aim of this retrospective study is to evaluate the clinicopathological features and outcome of patients (pts) with PTL.

Material: Between 1992-2007, 79 pts (51M/28F) were diagnosed and treated at our center, representing 11% of all NHL. Pts with leukemic PTL are excluded. The median age was 58 (range: 15-81) years. 56 (79%) had nodal PTL (23M/36F, 15AILD, 16SALCL and 19 (25%) extranodal. Fifty pts (67%) presented with clinical stage III-IV, 34 (46%) had B symptoms and 41 (52%) IPI =3. The commonest extranodal site was skin (14 nodal/11 extranodal) and among them with nodal T-NHL, 11 had >=2 extranodal sites. Overall 12 had bone marrow involvement. Autoimmune disorders were noticed in 8 pts. The first line chemotherapy (CT) was: 55 (73%) CHOP, 9 PROMACE-CytaBOM, whereas IFRT +/- CT was given in 11pts.

Results: After initial therapy 45 (37 nodal & 8 extranodal) were in CR, 4 in PR, 21 had stable disease, whereas occurred 5 early deaths. Twenty responding pts relapsed with a median CR, 8 (range 1-73) months. Overall 44 pts who relapsed / failed initial therapy underwent salvage CT: 20 ESHAP, 9 HEP/ECVAD, 13 other and responded 22/6 with primary resistant disease and 13/18 with relapse. With a median time of follow up 27 (range 1-198) m, 25 are alive in CR and 3 with disease. Five underwent autologous transplantation and 2 of them are in ongoing remission. The 3y OS, PFS is 48%, 36%, 37% respectively. Pts with bone involvement had 3y OS 24% and 3y OS is 22%. Significant differences were noticed among subgroups of nodal PTL, with better results for pts with SALCL: 3y: OS 85%, PFS 86%, DFS 87%, whereas no significant differences were documented between nodal-extranodal PTL. Pts with IPI<=2 had in 3y: OS=77% (p=0.0001), PFS=68% (p=0.0001), DFS=77% (p=0.013).

Conclusion: Conclusion: These uncommon types of NHL affect usually elderly men with advanced disease. The clinical course is often aggressive and half of pts failed initial therapy or relapsed in the first year. Better outcome was registered for pts with SALCL, without bone marrow involvement and IPI <2. The application of molecular and immunophenotypic markers may perim the development of new and more effective therapies in future.

516 ADULT T-CELL LEUKEMIA / LYMPHOMA: 10-YEAR-EXPERIENCE IN A PERUVIAN CENTER

N. Valdiviezo1, L. Casanova1, C. Samanez1, C. Flores1, J. Vidal1, C. Salatana1, M. Huairanga1, J. Leon1
1Medical Oncology Department, Instituto Nacional de enfermedades Neoplásicas, Lima, Peru

Background: Adult T-Cell leukemia/lymphoma (ATL) is an aggressive lymphoproliferative malignancy with different clinical characteristics and short survival, with an incidence of about 5% in HTLV-infected people. South American countries have reported the presence of HTLV-I, but the highest prevalence proportions of infection among the general population (1% to 5%) have been described in Brazil, Colombia and Peru. The objective was to determine the clinical features, received treatment and response in these patients.

Methods: We reviewed 188 clinical records of patient with HTLV-I infection, diagnosed at IDEN between 1995 and 2005, 150 of three patients had the diagnosis of ATL. We described clinical characteristics, treatment and response.

Results: 62.1% the patients had ATL-typical lymphoma, 36.6% acute type and 1.3% chronic type. The median age was 53 years (20-89), 51% were female. The clinical characteristics were: WHO 11/2 (56%); clinical stage III-IV (80%); symptoms (58%); increased DHL (74%); leucocytosis (50%); hypercalcemia (46%) and anemia (36%). In the ATL-lymphoma type patients, the most common primary localization was peripheral lymph node (80.6%), and the first extranodal sites were skin, stomach and nasopharynx (14% each one). 122 patients (80%) received treatment: chemotherapy (CT) 97% and radiotherapy (RT) 15.3%; CHOP was the most frequent CT scheme (89%). 21 patients (17.6%) with ct had complete response and 25% partial response; 76% of patients who achieved CR had recurrence. OS is being evaluated.

Conclusions: In our population, the ATL-lymphoma type was the most common subtype with 20% of primary extranodal disease; the response to CHOP chemotherapy was poor. Further studies must be done to determine whether either approach will have a significant impact on the illness since treatment of ATL patients is ineffective.