been significant prognostic factors for survival. 5-y RFS in pts who received RT was 51% and in pts treated with CT alone was 32% (p=0,0767). RT appeared to improve survival in pts who did not received full CT course, without CR and in pts with low and intermediate IPI risk categories.

Conclusions: In pts with advanced high grade NHL we obtained 45,7% 5yOS and 38,4% 5-y RFS. In patients irradiated post CT 5-y RFS was 51%. RT improves survival in selected pts categories.

1020 POSTER

Evolution of lymphocytopenia prognostic value in advanced Hodgkin's disease: a single-center experience.

T. Bogatyreva, O. Konova, V. Pavlov. *Medical Radiological Research Center, Radiation Therapy Dept., Obninsk, Russian Federation*

Background: Lymphocytopenia (lymphocyte count <600/mm^3 or <8% of WBC, or both) is one of seven factors combined into a prognostic score according to International Prognostic Factors Project. In attempt to separate a distinct group of patients with advanced Hodgkin's disease (HD) at very high risk of early progression, we retrospectively evaluated 1070 patients with stage III-IY and/or bulky and/or B-symptoms HD, referred to our Department between 1976 and 2000.

Methods: In order to analyze the incidence and significance of lymphocytopenia (LP) for clinical outcome the patients were divided into three subgroups according to one of three LP criteria: decrease of both absolute and relative counts (gr. 1, 32 patients); only relative LP (gr. 2, 43 patients); only absolute LP (gr. 3, 28 patients). All patients were treated with at least six courses of chemotherapy (COPP alone until 1988 in 597 patients; alternating or hybrid COPP/ABVD since 1989 in 474 patients) with or without radiotherapy. Clinical outcome in terms of freedom from progression (FFP) and overall survival (OS) were compared between the three groups. All patients were followed until death or at least for two years.

Results: The distribution of LP incidences was similar within the two historical series; the three groups accounted for 3%, 5% and 2% of total study population, respectively. There were at least 50% overlaps with other prognostic factors in each group, forming characteristic clusters: in gr. 1 - Hb < 10.5 g/dl was found in 50-70% of cases; in gr. 2 60-80% of patients were males with WBC > 15.0/mm^3; gr. 3 was presented by patients of age > 45 years (43%), males (43%), with Hb < 10.5 g/dl (50%). Still the treatment outcome during first decade was similar in all three groups (FFP at 2 years was 30%, 5 year OS was 50%) and during second decade the outcome in gr. 1 did not improved. Meantime the outcome in patients of gr. 2 and gr. 3 was clearly improved during the second decade (FFP at 2 years 78% vs 36% and 100% vs 33%, respectively; 5 year OS 83% vs 51% and 100% vs. 50%, respectively).

Conclusions: Combination of absolute and relative lymphocytopenia appears to be strong factor of adverse prognosis deserving further attention.

1021 POSTER

The role of hepatitis C virus (HCV) treatment in HCV-related B-cell non-Hodgkin's lymphoma (NHL)

D. Vallisa, P. Bernuzzi, E. Anselmi, A. Arcari, R. Bertè, L. Bidin, A. Lazzaro, C.F. Moroni, M. Palladino, L. Cavanna. *Hospital "Guglielmo da Saliceto", Medical Oncology and Hematology, Piacenza, Italy*

We have previously shown an epidemiological link between HCV infection and B-cell NHL in our geographical area. Indeed, some biological observations so far may indirectly suggest a link between virus and lymphomagenesis, such as the ability of lymphomatous cells to bind viral E2 envelope protein. Furthermore, recently, antiviral therapy against HCV revealed to be efficacious also against HCV-related splenic lymphoma with villous lymphocytes. In January 2001 we planned to test the effect of anti-HCV therapy on indolent low grade B-cell lymphoma (according to REAL classification) both at diagnosis and at relapse. Patients were requested to have well measurable nodal or extranodal disease, during the study no chemotherapy was allowed. Treatment consisted of pegilated alpha-interferon 50 microgram once a week and daily ribavirin 1 gr a day. Up to now, among the 5 patients entered the study. Three patients are evaluable. The first patient was enrolled in January 2001 while showing marginal zone nodal lymphoma that interested preauricolar and mammary lymph nodes together with bone morrow localization (40%). She was born in 1959. Since 5 years before she was affected by chronic viral C hepatitis with minimal activity (bioptic diagnosis), genotype 2a/2c. She began the treatment while showing an HCV viral load of 17820000 Eq/ml. During treatment lymph nodes disappeared and after 6 months bone marrow localization showed a decrease of 50% (good partial response), at the same time viral load disappeared. The second patient, enrolled in August 2001, showed a nodal relapse after one and half year of a previous marginal zone mucosa associated lymphoma of the palatum. The relapse concerned numerous retroperitoneal nodes with a maximum diameter of 2,5 cm and bone marrow. The patient was affected by chronic active viral C hepatitis from 1993 with about a 3-time increase of transaminases. After 6 month of treatment viral load was decreased of about 3 logs, marrow involvement disappeared such as retroperitoneal involvement (complete remission). The patient experienced grade III toxicity for platelet and white blood cells, which improved with reduction of dosage. The third patient partially evaluable is a woman 72 years old, affected by chronic viral C hepatitis (genotype 2a; ALT and AST in normal range) that showed in December 2002 the third relapse of follicular cutaneous lymphoma so she also underwent PEG-Intron and ribavirin. Now is under treatment with a decrease of cutaneous lesions. This experience proves that efficacious antiviral treatment in HCV related indolent lymphoma might modify the course of the lymphoma.

1022 POSTER

Dexamethasone, etoposide, ifosfamide, and cisplatin (DVIP) as salvage therapy in low- grade Non Hodgkin's lymphoma (NHL), following prior anthracycline containing therapy

N. Haim[1], A. Agbarya[1], L. Leitzin[1], M. Ben-Shachar[2], R. Epelbaum[1]. *[1] Rambam Medical Center And Faculty of Medecine-Tech, Oncology, Haifa, Israel; [2] Naharya Hospital, Oncology, Naharya, Israel*

Introduction: The combination of dexamethasone, etoposide, ifosfamide, and cisplatin (DVIP) was shown to be active in histologically aggressive NHL following prior therapy that included doxurubicin (Haim et al. Cancer 80:1989, 1997). We, therefore, evaluated DVIP as a salvage chemotherapy following prior anthracycline containing therapy in patients with low- grade NHL.

Patients and Methods: Original DVIP consisted of dexamethasone 20mg x 2, days 1-4, etoposide 75mg/m2, days 1-4, ifosfamide 1200mg/m2, days 1-4, and cisplatin 20mg/m2, days 1-4. All drugs were given IV,and cyles were repeated every 3 weeks. Initial drug doses were reduced according to standard criteria and ranged between 10%-100%, median 60%. Between May 1990 and June 2002, 44 patients (23 males and 21 females, age: 29-84, median age 61 years), with histologically confirmed low- grade NHL were treated with DVIP at our center.The most common histological subtype was follicular small cleaved (Working Formulation), (20 patients, 45%) . Prior therapy included two or more combinations in 32 patients (73%), WHO performance status was grade 2 or more in 27 patients (61%), serum LDH was elevated in 18 patients (41%). Eighteen (41%) had B symptoms and 8 patients (18%) had bulky disease.

Results: All patients were evaluable for toxicity, and 42 were evaluable for response. Partial response (PR) was achieved in 14 patients (33%) ,and complete response (CR) in 13 patients (31%) (overall response rate 64%). Complete response rate was higher among patients who had achieved CR with prior therapy compared to those who had not achieved CR (11/26, 42% vs. 2/18, 11%). Median survival time was 12 months for the entire group and 114 months for complete responders.

The main toxicity of DVIP was myelosuppresion. Grade 4 leukopenia was noted in 9 patients (20%), grade 4 thrombocytopenia was in 3 patients (7%), and grade 4 anemia was in 3 patients (7%). Neutropenic fever that required IV antibiotics developed in 8 patients (18%) and in 8/186 cycles (4%) .Red blood cell transfusion was required in 7 patients (16%) in 11 cycles (6%). Due to myellosuppression further dose reductions were required in most patients. Non- hematological toxicity was moderate. There were no drug related deaths.

Conclusions: DVIP is active regimen in low-grade NHL following prior anthracycline-containing chemotherapy, and might induce durable remissions.

1023 POSTER

Analyses of percentage CD23 cell membrane molecule expressed in ratio to the immunoglobulines concentration in B-CLL.

V. Jurisic[3], M. Colovic[1,2], N. Colovic[1], N. Kraguljac[1]. *[1] Insitute of Hematology, Clinical Center of Serbia, Belgrade, Yugoslavia; [2] University of Belgrade, School of Medicine, Belgrade, Yugoslavia; [3] University of Kragujevac, School of Medicine, Kragujevac, Yugoslavia*

Background: B-CLL is a malignancy characterized by accumulation of terminally differentiated B cells. However, with increasing number of peripheral lymphocyte number (PBL) and advance stage of disease, usually

enlargement of a-functional cell number was accompanied. To estimated B-cell functional activity of circulated PBL in terms of high presence or absence of the normal cells pool, we analyzed association of CD23 membrane molecule expression on cell surface membrane in terms of serum concentration of imunoglobulins classes of IgM, IgG, IgA.

Material and methods: Study included 77 B-CLL patients, diagnosed by classical criteria including FAB and Binet staging system with immunophenotyping procedure by Flow cytometry on FACScalibur (Becton-Dickinson, San Jose, USA) using panel of monoclonal antibodies (anti-CD5, CD10, CD19, CD20, CD21, CD23, CD38 and HLA-DR) for cell membrane molecule expression evaluation and B-CLL disease confirmation. The functional activity of circulated B lymphocytes was done by determination sera concentration of immunoglobulin classes IgM, IgE and IgG using RID plates (Behring, Germany).

Results: The results showed significant decrease of IgM concentration with disease progression based on FAB and Binet clinical classification. In addition, individual analyses of CD23 expression in terms of the functional activity of B cells showed a strong correlation with decrease of IgM concentration (Pearson correlation, $p<0.05$), but no with IgG or IgE. Since patients in advance stage of disease showed some immune system disturbance and consequently recurrent bacterial infections we confirmed in disease progression simultaneously decrease of CD23, a negative disease prognostic marker associated with low IgM.

Conclusions: This finding were probably consequence of large number of tumor cells and low of normal cells without possibility for discrimination its, based only on B cell marker presence expression, (high expression of CD5), but partly confirmed and better explained in association with low IgM production.

1024 POSTER

Etoposide, Platinum, Ifosfamide and Dexamethasone (EPID) as second line treatment in patients with non-Hodgkin's lymphoma (NHL)

F. Aldaco, A. Gomez, M. Cerna, L. Vazquez, M. Valdez, G. Sanchez, A. Erazo, G. Cervantes, L. Torrecillas, P. Cortes. *CMN 20 NOviembre, Clinical Oncology, México city, Mexico*

Background: The NHL are becoming an increasingly common cancer, but only 40-50% patients are cured with current regimens. Patients relapsing have a poor prognosis and chemotherapy usually incorporates drugs such as cisplatin and etoposide (CE). The use of CE plus Ifosfamide and Dexamethasone could increase the response in NHL. Aim. To evaluate the efficacy and safety of EPID as second line in pts with NHL. Patients and methods: We included pts with NHL, failure or relapse after to CHOP, measurable disease, ECOG 0-2. Treatment: Etoposide 80 mg x m2 d 1-3, Platinum 80 mg x m2 delivered in 3 days, Ifosfamide 5000 mg x m2 delivered in 3 days and Dexamethasone 16 mg iv d 1-3 every 3 weeks.

Results: We included 30 pts, median age 52 years (range 21-76), stage III/IV 46%, extra nodal 8%, histological type (working formulation): LG 20%, I 69%, HG 11%, median time to progression or failure with CHOP 8.2 months. The Overall response rate was 73% (CR 35% and PR 38%) and SD 12%. Pts with CR the time relapse was 18.2 months, in patients with PR time to progression was 6.6 months. Overall survival (OS) was 16.6 months. The 2 years overall survival was 26%, and for pts with CR was 45%. Toxicity grade 3/4 (WHO criteria): neutropenia 56%, febrile neutropenia 15%, anemia 18%, thrombocytopenia 15%, mucositis 7%, nausea and vomiting 31% and diarrhea 3%. There was one related to treatment death associated with febrile neutropenia.

Conclusion: EPID is an active regimen in NHL with good response (73%) and toxicity manageable. Pts with CR (1/3) the OS is excellent. Large studies are required to establish the therapeutic potential but this regimen appears to be a reasonable option.

1025 POSTER

Long-term outcome and mortality trends in follicular lymphoma treated with radiation therapy

B.A. Guadagnolo[1], S. Li[2], D. Neuberg[2], A. Ng[3], L. Hua[3], B. Silver[3], M.A. Stevenson[4], P. Mauch[3]. *[1] Joint Center for Radiation Therapy, Radiation Oncology, Boston, MA; [2] Dana-Farber Cancer Institute, Biostatistical Science, Boston, MA; [3] Dana-Farber/Brigham and Women's Cancer Center, Radiation Oncology, Boston, MA; [4] Beth Israel Deaconess Medical Center, Radiation Oncology, Boston, MA, USA*

Background: Early stage follicular non-Hodgkin's lymphoma (NHL) is associated with prolonged survival but a high likelihood of relapse. We reviewed the long-term treatment outcomes, prognostic factors, and competing causes of death in patients who received radiation therapy either alone or in combination with chemotherapy as initial therapy for their localized follicular NHL.

Materials and Methods: Between 1972 and 2000, 106 patients presented with stage I-II, grade 1-2 follicular NHL and received radiation therapy alone or combined chemotherapy and radiation therapy at our institutions. Patients previously treated for NHL were excluded from the analysis. The median age at diagnosis was 55 years (range 21-93). Seventy-four percent had stage I disease, and 26% had stage II disease. Histology was grade I in 66% and grade 2 in 34%. Extranodal disease was present at diagnosis in 27%. Tumor size was $\leq$ 3 cm in 53% and >3 cm in 47%. Seventy-six percent were treated with radical radiation therapy alone, and 24% received combined chemotherapy and radiation therapy. Median radiation dose was 36.6 Gy. Overall survival (OS) and freedom from treatment failure (FFTF) were estimated using the Kaplan Meier method. Survival curves were compared using log-rank tests. A Cox proportional hazards model was used to determine predictive factors.

Results: Median follow-up was 12 years (range 0.5-26). The median survival time was 19 years. The 5-, 10-, and 15-year OS rates were 93%, 75%, and 62%, respectively. On both univariate and multivariate analysis, age $\geq$ 60; was the only significant adverse prognostic factor with respect to OS, with 15-year OS rates of 72% for age <60 and 43% for age $\geq$ 60 (p=0.001) (Hazard ratio [HR]=3.04; 95% CI 1.45-6.39; p=0.003). There were 35 deaths; causes were NHL (19), second malignancy (6), cardiac disease or stroke (3), and unknown (7). FFTF rates at 5, 10 and 15 years were 72%, 46%, and 39%, respectively. Relapse data were available for 97 patients, of whom 47 (48%) relapsed. Seven patients recurred within the initial radiation field. No factors were significantly predictive for FFTF on univariate analysis. On multivariate analysis, tumor size >3 cm was the only significant adverse factor for FFTF (HR= 1.98; 95% CI=1.04-3.79; p=0.04).

Conclusions: Age <60 years was associated with better overall survival, and patients with tumors $\leq$ 3 cm had a lower risk of relapse or death from NHL. Stage, grade, presence of extranodal disease, and treatment with chemotherapy did not have a significant impact on relapse rates or overall survival. Although patients with early stage follicular lymphoma have a long median survival, the leading cause of death to date remains NHL.

Imaging

1026 POSTER

In vivo monitoring of NK cell mediated host defence against lung micrometastasis using positron emission tomography (PET) and [^{18}F]-2-deoxyglucose (FDG)-labeling of tumor cells

Y. Hama[1], C. Kruschinski[1], S. von Hörsten[1], M. Zielinska-Skowronek[2], W. Knapp[3], B. Vaske[4], R. Pabst[1], R.E. Schmidt[2], M. Hofmann[3]. *[1] Medical school of HannoverMedical school of Hannover, Functional and Applied Anatomy, Hannover, Germany; [2] Medical school of Hannover, Clinical Immunology, Hannover, Germany; [3] Medical school of Hannover, Nuclear Medicine, Hannover, Germany; [4] Medical school of Hannover, Biometry, Hannover, Germany*

Background: Recently we have demonstrated very rapid cellular host defense mechanisms against transplanted syngeneic mammary adenocarcinoma cells in the lungs of F344 rats using immunohistological and vital dye labeling techniques. Already minutes after tumor cell inoculation, a significant increase of NK cell to tumor cell co-localizations was found in the histological work up of lung tissue. However, direct in vivo evidence on the early kinetics of the cellular host defense against metastatic cells is lacking. Here we report direct in vivo monitoring the kinetics of NK cell dependent tumor cell lysis using dynamic PET-scanning of 2-18F-deoxyglucose (FDG) labeled tumor cells in the lungs of either NK cell depleted or intact F344 rats.

Materials and methods: Cultured MADB106 tumor cells were labeled by incubation with FDG and Insulin (1U/l) and injected via the lateral tail vein of F344 rats. Lysis of the in vitro-loaded tumor cells was then monitored via dynamic PET scanning up to 45 minutes following injection. Animals that had received NK cell depletion with mAb 3.2.3 two days earlier were investigated as well as sham-treated control animals (each n = 6). After depletion, no NK cells were detectable by immunohistology in lungs. Sets of 2 depleted versus 2 intact animals were scanned simultaneously using a specialized holding device in a standard human PET scanner (Hr+, Siemens/ CPS; 3D mode). Lung time activity functions were evaluated by means of ROI technique.