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.

Results: In this model of lung metastasis, tumor cells rapidly accumulate in the lungs and do not seed in other organs. After tumor cell inoculation the activity per ROI peaked within 2-5 minutes, followed by a gradual down slope. Statistical analysis using a linear mixed model revealed a significantly accelerated decrease of lung time activity in sham controls compared to NK depleted animal (coefficient of slope: -0.66 vs -0.54).

Conclusions: For the first time we provide direct evidence for a very rapid NK cell mediated lysis of tumor targets in vivo and in an individual organ, we conclude that a functional in vivo monitoring of FDG-labeled tumor cells represents a promising approach to gain more insight into the kinetics of the mechanisms of metastasis formation and related cellular host defense processes.

1027 POSTER

Evaluation of pulmonary lesions using ^{99m}Tc-depreotide and ^{201}Tl-chloride. Preliminary results

D. Boundas[1], N. Karatzas[1], K. Pistevou-Gompaki[2], G. Sarikos[3], Z. Kalaitzi[2], D. Papanicolaou[4], D. Ekonomidis[4]. [1] *Aristotle University Medical School, Hippokration Hospital, Nuclear Medicine Department, Thessaloniki, Greece;* [2] *Aristotle University Medical School, AHEPA Hospital, Department of Radiotherapy-Oncology, Thessaloniki, Greece;* [3] *Theagenio Anticancer Hospital, Department of Pneumonology-Oncology, Thessaloniki, Greece;* [4] *Aristotle University Medical School, Hippokration Hospital, Second Department of Internal Medicine, Thessaloniki, Greece*

Background: Recent reports have indicated the value of ^{99m}Tc-depreotide, a labelled somatostatin analogue, in the evaluation of pulmonary nodules. ^{201}Tl-chloride has been for long and applied in the diagnosis of lung cancer. The purpose of this study is to compare the diagnostic potential of ^{99m}Tc-depreotide and ^{201}Tl-chloride in the evaluation of pulmonary lesions.

Material and Methods: Eighteen patients (mean age 62.3±9.4 yrs, 5 female) with 28 pulmonary lesions suspect for malignancy were submitted, on separate days,to ^{99m}Tc-depreotide and ^{201} Tl-chloride SPECT. Early (15 min) and delayed (3 hours) scans were acquired for each radiopharmaceutical. Tumor-to-contralateral normal lung activity ratio for both early (early ratio, ER) and delayed (delayed ratio, DR) scans were calculated and the retention index [RI = ((DR-ER)/ER)*100] was derived. Lesions were characterized as benign (9/28) or malignant (19/28) on the basis of histological examination, and/or clinical and radiological follow-up. Differences between benign and malignant lesionsí characteristics were examined by means of non-parametric Mann-Whitney statistics and linear regression analysis was used for correlations between radiopharmaceuticals.

Results: All malignant lesions accumulated both tracers. Six out of nine benign lesions were ^{201}Tl-negative. Four out of nine of them were also ^{99m}Tc-depreotide-negative, the rest showing minor accumulation of tracer. However, ER and DR of both agents were significantly different between benign and malignant lesions (^{99m}Tc-depreotide ER, 1.27±0.37 vs 2.81±0.60, $p<0.001$; ^{99m}Tc-depreotide DR, 1.40±0.45 vs 3.58±0.83, $p<0.001$; ^{201}Tl ER, 1.12±0.29 vs 2.57±0.66, $p<0.001$; ^{201}Tl DR, 1.06±0.15 vs 2.48±0.57, $p<0.001$). For each radiopharmaceutical ER was well correlated to DR (r=0.88 for ^{201}Tl and r=0.86 for ^{99m}Tc-depreotide) . Inter-agent correlation was fair for both scan phases (r=0.65 for ER and r=0.64 for DR). Interestingly, RI of both agents did not show any statistically significant difference between benign and malignant lesions or any inter-agent correlation.

Conclusion: These preliminary results show that ^{99m} Tc-depreotide may recognize malignant lung lesions as effectively as ^{201} Tl, having the advantages of improved image quality and favourable dosimetry. Semiquantitative analysis may be helpful in discrimination between benign and malignant lesions.

1028 POSTER

Contrast-specific ultrasound (CS-US) in staging and follow-up of splenic lymphomas

R. Lo Bianco[1], S. Tafuto[2], O. Catalano[1], M.L. Lentini Graziano[2], A. Siani[1], S. Quattrin[2]. [1] *S. Maria delle Grazie H., Diagnostica per immagini e Radiologia Intervenstis, Pozzuoli (NA), Italy;* [2] *S. Maria delle Grazie H., Oncoematology, Pozzuoli (NA), Italy*

Aims: To illustrate our experience in the evaluation of splenic hematological malignancies with a real-time, CS-US mode.

Material and methods: January to December 2002 we studied 25 patients (10 with Hodgkin disease and 15 with non-Hodgkin lymphoma): 14 M and 11 F aged 28-79 years. After a baseline US study we rapidly injected 2.4-4.8 mL of the second-generation microbubble agent SonoVue® (Bracco). Contrast-enhanced studies were carried out with a contrast-specific software (CnTI - Contrast Tuned Imaging, Esaote) using a continuous-mode, harmonic acquisition and a low acoustic pressure. US studies outcome was retrospectively correlated with the results of standard tools, including CT (13 cases), MRI (1), US follow-up (10), and FNAB (4).

Results: Among 16 cases with focal involvement contrast-enhanced US detected 47/52 lesions demonstrated altogether by reference tools. Conventional US recognized 35/52 lesions.Lesion extent defined by CS-US correlated with standard tools, being similar (81% of cases), underestimated (13%), and overestimated (6%). Baseline US defined the lesion size correctly in 56% of cases, underestimating in 31% and overestimating in 13%. Lesion-to-parenchyma contrast of CS-US resulted low (11% of cases), intermediate (62%), and high (27%). Conspicuity at conventional US was low (52% of cases), intermediate (33%), and high (15%). Lesions appeared as constantly hypoechoic (hypovascular), better definable during intermediate-delayed phase of enhancement than on early phase. Arteries were visible around the lesion and perpendicularly entering along intralesional septa. A clear intralesional microcirculation was visible. Among 9 subjects studied after chemotherapy, loss of microcirculation and marked lesion hypoechogenicity were visible in case of response. Hence, the disease activity could be assessed. In 9 patients with diffuse disease we recognized a slightly less intense and persistent parenchymal opacification, suggesting the need for a full, 4.8 mL contrast medium dose.

Conclusion: The spleen is an optimal target CS-US, being superficial, highly vascularized, relatively small, and homogeneous. Contrast-enhanced, gray-scale US is a simple and poorly-invasive tool in morphological and functional imaging of lymphomatous disease.

1029 POSTER

Quantification of microvasculature in cervix carcinoma with functional CT imaging

I. Yeung[1,5], J. Darko[2], M. Haider[3], M. Milosevic[4,5], A. Fyles[4,5]. [1] *Princess Margaret Hospital, Radiation Physics, Toronto, Canada;* [2] *Kingston Regional Cancer Centre, Medical Physics, Kingston, Canada;* [3] *Princess Margaret Hospital, Diagnostic Imaging, Toronto, Canada;* [4] *Princess Margaret Hospital, Radiation Oncology, Toronto, Canada;* [5] *University of Toronto, Radiation Oncology, Toronto, Canada*

Background: Functional CT (fCT) imaging has been commonly accepted for clinical practice in a few selected anatomic sites such as the brain. The fCT method is based on dynamic CT scanning on the volume of interest post intravenous injection of X-ray dye. The arterial and tissue uptake curves of dye can be obtained from the dynamic CT images and they are applied to tracer kinetics models based on which physiologic parameters are determined. This pilot study is to demonstrate the feasibility of fCT on cervix carcinoma applied to the "distributed capillary adiabatic tissue homogeneity" (DCATH) model we previously proposed [1]. The fCT parameters were also compared to oxygenation (PO2) and interstitial fluid pressure (IFP) measurement.

Material and Methods: A group of 20 patients with cervix carcinoma took part in a pilot study of fCT at time of disease staging prior to radiation therapy. They were scanned with a GE Light Speed CT scanner and cine technique factors of 120 kVp, 100 mA, 1s rotation for 120 s. The data were downloaded to a SUN BLADE 1000 workstation for analysis with a nonlinear deconvolution method using the quasi-Newton algorithm. The DCATH model calculated 5 fCT parameters; namely, blood flow (BF), capillary permeability surface area product (PS), blood volume (BV), mean transit time (MTT) and transit time spread (TTS). The advantage of this model is that TTS measures the architecture complexity of microvasculature in the tissue. Seventeen patients also received IFP measurement by a sick-in needle technique while 15 patients had PO2 measured with the Eppendorf probe. The fCT parameters were tested against IFP and PO2 for correlation.

Results: The average fCT parameter estimates for tumor are: BF = 62.7±21.3 ml/min/100g, PS = 25.2±11.1 ml/min/100g, BV = 11.5±4.0ml/100g, MTT=12.1±3.5s and TTS=5.3±1.3s. The average measured IFP and PO2 are 18.2±8.9 mmHg and 17.3±18.2 mmHg respectively. None of the fCT parameters indicated strong correlation with IFP or PO2 and the only significant correlation is between BF and mean PO2 (r=0.46). However, BF was found to strongly correlate with the slope of tissue uptake curve (r=0.85).

Conclusions: The feasibility of the fCT method was demonstrated and average values of the fCT parameters were obtained in this group of patients with cervix carcinoma. The initial slope of the tissue uptake curve may be a good relative measure of BF because of their strong correlation. The weak correlation between BF and PO2 suggests that tissue oxygenation is somewhat dependent on supply via blood flow into the tissue but perhaps