OS for stage I, II1, II2, and IV were 75%, 67%, 29%, and 30%, respectively. Five-yr OS for low-risk, intermediate-risk and high-risk pts were 74%, 30% and 0% (p = 0.02). The independent prognostic factors were age (p = 0.03), PS (p = 0.01), stage (p = 0.01), B-symptoms (p = 0.05), and LDH level (p = 0.01). Primary site (small vs. large bowel; p = 0.34), CHT regimen (CHOP vs. MACOP-B; p = 0.35) and surgical radicality (p = 0.44) did not influence outcome. Bulky disease was related to lethal toxicity (X2; p = 0.05).

Conclusions: A limited surgical resection followed by anthracycline-containing CHT was an effective and safe treatment for pts with stage I or II1 PAWIL subtype DLCL. Pts with stage II2 had a worse survival, which may be explained by the high incidence of lethal complications observed in cases with bulky disease that underwent a more extensive resection. Since surgical radicality does not influence survival, to restrict debulking to the site of high risk of perforation is advisable to avoid lethal complications and CHT delay. Pts with AD should be managed with an IPI risk-related therapy, taking into account that one third of relapses, especially in pts with bulky disease and very high LDH levels, involved the CNS. These observations deserve to be confirmed, and their therapeutic relevance defined, in a larger multicentric series.

1347 POSTER

Extranodal Non-Hodgkin's lymphoma of the testis

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This study covers a period of 96 months, during which 396 patients aged 11–80 and suspected of having testicular tumor underwent orchidectomy. After rapid section diagnosis, all patients underwent inguinal semi-castration with ligature of the spermatic cord. After final diagnosis of malignant lymphoma and its classification, precise staging was conducted. Once the individual stages were determined (all were IE), 19 of the 20 patients were administered CHOP polychemotherapy: 750 mg/m^2 cyclophosphamide were quickly injected i.v. on Day 1; 50 mag/m^2 adriamycin i.v. as a bolus injection on Day 1; 1.4 mg/m^2 vincristine i.v. (for a maximum of 2 mg/m^2) as a bolus injection and 100 mg of prednisone orally on Days 1–5. This therapy regimen was administered every 28 days for a total of four courses. One of the 20 patients received only radiotherapy of the para-aortal and pelvic lymph node with 3600 cGy. Staging examinations were conducted every three months on all of the patients. 17 of the 20 patients evinced a highly malignant B-cell type Non-Hodgkin's testicular lymphoma; 14 of the patients had a centroblastic lymphoma; 3 of the 20 were diagnosed with immunoblastic lymphoma; and one patient had a highly malignant T-cell lymphoma. Surprisingly, two patients evinced pleomorphic immunocytoma which contained, however, a very high proportion of immunoblasts, some of which were already differentiating into immunoblastoma. For 19 of 20 patients, staging examinations showed that only one testicle was afflicted; while in one patient, both testicles had been simultaneously infiltrated by centroblastic Non-Hodgkin's lymphoma, although here as well, no other organs had been affected, Hence, stage IE applied to all 20 patients. The median age of the patients with extranodal testicular lymphoma was 57.3. During the 96-month period of observation, no relapses occurred. After four years, one patient did have a cerebral neuroblastoma, to which he succumbed. The remaining 19 patients are still alive, and in none of them has a tumor relapse or remote metastasis been found thus far.

1348 POSTER

Bone marrow biopsy in patients with Hodgkin's disease (HD): Is gold standard really gold?

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Purpose: Bone marrow (BM) biopsy is still used as an essential part of staging of patients with HD. The aim of this retrospective study was to determine how many cases of BM invasion call be missed by routine BM biopsy.

Materials: Unilateral Jamshidi BM biopsy was obtained from the posterior iliac crest of 44 patients with HD. Diagnostic sings of BM invasion were as follows: findings of Red-Sternberg cells or their mononuclear variants within a suitable cellular background and/or areas of extensive fibrosis. Whole body BM scintigraphy (BMS) was performed within 2 weeks of BMB. In all but four cases of negative biopsy and positive scintigraphy BM invasion was proved by concordant abnormalities on any of the following examinations: MRI, bone scanning, X-ray and CT.

Results: In accordance with above mentioned criteria BM invasion by HD was diagnosed in 22 of 44 evaluated cases. Ten patients had positive BM biopsy: Red-Sternberg cells were revealed in only 4 observations. BMS was abnormal in 25 cases: 9 of them were concordant with BMB, 12 – with additional examinations and 4 – remained equivocal (false-positive). Twelve of 22 patients with BM metastases were missed by BMB. It's sensitivity was equal to 45.4%.

Conclusion: Because of very low sensitivity BM biopsy can't be used as a gold standard for diagnosis of BM invasion by HD. Whole body BM visualisation is obligatory for accurate staging in this category of patients.

1349 POSTER

The expression of cell cycle regulators p27 and pRh in low grade and high grade Non-Hodgkin's lymphomas (NHL)

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Purpose: Pathologist today use advanced methodology in diagnosing NHL, but it is still complicated and spesific markers are needed to improve the classification accuracy for targetting various treatments for different subgroups. The purpose of this study was to investigate the role of cell cycle regulators p27 and pRb in grading of the lymphomas.

Methods: The samples of 104 adults with high or low grade NHL were evaluated. The cases were classified histologically according to the REAL by an experienced pathologist. The expression of cell cycle regulators p27, pRb and tumor proliferating marker Ki-67 was investigated with immunohistochemistry. Tumor samples with p27 and pRb staining were graded into four groups (from negative to high expression). Ki-67 staining was evaluated by counting a percentage of proliferating cells.

Results: All differences in expression of p27, pRb and Ki-67 compared to histological grading of lymphomas were statistically significant ($p < 0.05$). The percentage of proliferating cells increased as p27 expression was lost ($p < 0.0001$). The opposite behaviour was seen when observating pRb against Ki-67 ($p < 0.0001$). Low grade lymphomas showed marked expression of p27 and were usually negative for pRb whereas high grade malignancies were negative or showed only very low staining of p27 and high expression of pRb.

Conclusion: The expression of cell cycle regulators p27 and pRb correlates with the grade and proliferating status of the lymphomas.

1350 POSTER

Do combination of chemotherapy (CT) and radiotherapy (RT) modify the patterns of relapse and the late central nervous system toxicity (LCNST) in immunocompetent patients with primary cerebral non-hodgkin's lymphoma?

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Combination with high-dose CT directed towards the CNS followed by whole grain RT are known to improve survival but also could modify the pattern of relapse and induce neurodegeneration in pts with PCNHL. This study reports the patterns of failures and LCNST in pts prospectively treated with the same CT/RT combination at the IGR from 01/90 to 11/97: 21 HIV-negative pts, M/F: 12/9, median age 56 (16–68), PS-WHO 0–1: 14 pts, 2–3: 7 pts. PBNHL diagnosis obtained by stereotaxic: 14 pts, or surgical biopsy: 7 pts revealed large B cell (20 pts) and anaplasic NHL (1 pt). CSF was involved in 1 pt and CSF protein "0.6 g/l in pts. Lesions were unifocal (8 pts) or multifocal (13 pts). CT consisted of 2 to 3 monthly cycles (cy) with Methotrexate (MTX) (3 g/m^2 d1, 15), VM26 (100 mg/m^2 d2–3), BCNU (100 mg/m^2 d4), and methylprednisolone (60 mg/m^2 d1–5) ± GCSF along with 6 intrathecal CT of MTX and aracytine. Whole brain RT started 4 weeks after CT (40 Gy/20 f/28 d + 10–15 Gy boost on unifocal lesions). Four pts (20%) and 15 pts (67%) experienced complete response at the completion of CT and at the end of CT/RT, respectively. With a median follow-up of 22 months (mts) (1–59), 4/15 pts with CR (27%) relapsed, outside the primary site of the tumour (3 in another brain area and 1 in retroperitoneal lymph nodes). We observed 8 tumor-related deaths and 1 death due to LCNST. The 3-year survival was 63% and 12 pts were long term survivors (disease-free: 10 pts, with relapses: 2 pts). LCNST (RTOG/EORTC) started 6 mts after the end of RT in 13/15 pts (87%) (gr 1–2:10, gr 3:2, gr 4:1). In conclusion, combination

of CT and RT improved survival in pts with PCNHL. Despirte whole brain RT, patients with CR recurred within the brain, outside the primary site. As combined MTX and RT had adverse effects on cognitive functions, whole brain RT is questionable in pts with PCNHL

1351 POSTER

Primary breast lymphoma

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Background: Primary breast lymphoma is a rare disease, represents 0.1% of breast malignancies and 2.2% of all extranodal non Hodgkin's lymphomas. The literature has reported about 300 cases. We reviewed the experience of the Instituto de Enfermedades Neoplásicas (Lima-Peru) from 1952 to 1997.

Methods: We found 17 patients with primary breast lymphoma. Twelve received treatment in our institution, and 11 of this had complete treatment. The follow-up was from 12 to 120 months. The chemotherapy an radiation therapy were the elective treatment. Some patients were subject to surgery.

Results: All the patients were females. The mean age was 45.4 years (15–69 years). The mean period of disease was 3.9 months. The sympton was breast mass in 11 patients and 1 had skin erythema. The histologyc were: WF:G, 5 (41.7%); WF:A, 2 (16.7%); WF:H, 2 (16.7%); WF:B, 1 (8.3%); WF:I, 1 (8.3%); and WF:F, 1 (8.3%). 4 stage IE, 4 stage IIE, and 4 stage IVE. Of 11 patients who received complete treatment, Five patients were treated with CHOP and COPP. (3 patients with cytologyc diagnostic of carcinoma, receiving chemotherapy after surgery) Six patients received Chemo and radiation therapy; One patient died three years after received treatment for other cause, and 7 are alive at present time, all without disease evidence. Three patient after two years developed recurrence with subtype diffuse, large cell WF:G lymphoma. Of all patients who are alive or died without disease evidence, 2 were stage IE 3 stage IIE; and 3 were stage IVE with follow-up of 3 to 9 years. Of the 9 patients with 3 or more years of follow-up, 6 (66.7%) are free disease, and the 8 patients who are alive and coming to control, 5 (62.5%) are free disease at 5 or more years.

Conclusions: The diffuse, large cell WF:G lymphoma was the predominant histologyc subtype. The chemotherapy and radiation therapy are the treatment of choice with a 62.5% of survival at 5 years for any stage.

1352 POSTER

Bendamustine in the therapy of lowgrade malignant lymphomas

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Purpose: Palliative treatment of advanced low/intermediate grade lymphomas is charcterized by high remission rates, short remission duration and necessitiy of subsequent therapies. Lacking curability, quality of life is a major issue. A therapeutic option is the alkylating agent bendamustine (*be*); is associated with little toxicity and good tolerability, even in older patients. We present the data of a retrospective analysis of 34 patients, treated with be single agent or combination therapy with mitoxantrone (*mitx*).

Methods: 34 patients (age 48–82, mean 63) were treated with be (21) or *be/mitx*(13). Disease entities: follicle center (fc) 13, lymphoplasmocytic (lp) 9, lymphocytic (lc) 9, mantle cell (mc) lymphomas 2, plasmacytomas (pl) 3. Treatment: *be* 100 mg/m^2, d 1–3, with or without mitx 6 mg/m^2, d 1–2. Mean number of cycles was 3.8.

Results: Overall remission rate was 61% (29% CR, 32% PR); NC 24%, PD 15%. Results, discriminated by hisologic subtype: *CR:* fc 6, lp 3, lc 1; *PR:* fc 3, lp 2, lc 4, mc 2; *NC:* fc 2, lp 4, lc 1, pl 1; *PD:* fc 2, lc 1, pl 2. Remission duration was 8–11 months for patients with CR, PR and NC. *be* single agent therapy resulted in 48% CR/PR, the combination regimen in 69% CR/PR.

Toxicity: Hematologic: 8 cases of grade 3/4 leukopenia/thrombocytopenia. Nausea/emesis grade 2 was observed in 11 patients, grade 3 in 3 patients. Alopecia (g 3) was only seen in patient.

Conclusion: Be and *mitx* are effective drugs in the palliative treatment of low/intermediate grade malignant lymphomas. Single agent and combination treatment are well tolerated; dose limiting is hematotoxicity. To further define the role of bendamustine-based therapy, randomized studies, comparing it with actual standard treatment are necessary.

1353 POSTER

HCV and non-Hodgkin lymphomas: A retrospective study

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Purpose: As reported by several studies, the prevalence of HCV-infection in B-cell lymphoproliferative disorders (19%) appears to be significantly higher than in other hematological malignancies as in the general population (2.3%); the correlation emerges also from recent virological and histopathological data. In a retrospective study based on a series of 91 patients affected by B-cell non-Hodgkin lymphoma (NHL) or other lymphoproliferative disorders diagnosed in our Institution, the prevalence of HCV infection was evaluated.

Methods: HCV serological markers were investigated at diagnosis in 43 women and 48 men affected by B-cell lymphoma, except when a diagnosis of chronic HCV-related hepatitis was documented.

Results: 11 cases of a series of 91 consecutive patients resulted positive for serological markers of HCV-infection (12.1%). Among these 4 were low grade, 3 high grade, and 2 intermediate grade lymphomas second W.F.; the other cases included an angiotropic large cell lymphoma and an unclassified B-cell lymphoproliferative disorder.

Conclusion: These data are consistent with an association between HCV-infection and B-cell lymphoproliferative disorders. However the relevant diffusion of HCV-infection in South Italy (1–5%) and the small size of the study require further analysis to indicate a possible role of HCV in the lymphomagenesis.

1354 POSTER

Can we include apoptotic index in prognostic scores in patients with myelodysplatic syndrome

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Objective and Methods: To evaluate the prognostic significance of apoptotic index (AI) and to compare AI with other prognostic scores, Bornemouth (BS) and Spanish score (SS) in 30 patients MDS. The bone marrow samples of 30 pts. with MDS were embedded for semithin morphological analysis (Leukemia 1997) and number of cells in apoptosis were counted and expressed as percentage (AI). According to FAB there were RA and RARS (8 + 3 pts), RAEB + RAEB-t (14 + 2) and 3 pts with CMML. Analysis have been calculated on 50% survival basis ($SRV_{50\%}$).

Results: According to FAB, pts with low risk (RA + RARS) have significant better survival than RAEB/t (OS_{5y} 80% vs $SRV_{50\%}$ 20 m., log rank $p < 0.01$). We have introduced apoptotic prognostic score APS (low AI < 2.5, intermediate AI 2.5–3.99 and high AI > 4). In analysis of APS that patients with low APS survive better then others (>68 m) while pts with intermediate and high APS have worse survival (24 and 17 m). The survival according to APS was similar to survival according to BS and SS. We also found that pts. with low and high APS have significantly different BS (t test $p < 0.05$) but not SS.

Conclusion: Our analysis is influenced by the small number of analyzed patients but we think that apoptotic prognostic score with cutoff of at least of 3% of apoptotic cells (AI) can be used as a simple and reliable prognostic factor in patients with myelodysplastic syndrome and can be included in future prognostic score system.

1355 PUBLICATION

Antileukemic activity and induction of apoptosis by gemcitabine

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Gemcitabine (Gem) is a new deoxycytidine analog which inhibits cellular DNA synthesis by masked chain termination. We studied the cytotoxic efficacy of Gem by MTT-assay in human myeloid HL-60 and K-562 leukemic cells and by investigating DNA fragmentation. BCR-ABL positive K-562 cells were less sensitive to Gem then AML derived HL-60 cells. Gel electrophoresis of DNA isolated from Gem treated HL-60 and SKW-3 showed oligo-nucleosomal fragmentation typical for programmed cell death (5 μM for 20 h). Under the conditions of a cell-free system consisting of cytosolic