were in stage III according to Salmon/Durie, two had stage B. Five patients were pretreated, 2 with chemotherapy and 3 with radiation.

Four pts having received at least 2 cycles of CLAD are evaluable for response. Every pat reached a partial response (>50% reduction in m-protein). Median fall in M-protein after two cycles was 41% (range 30–49%). For safety 14 cycles were evaluated. Overall, treatment was well tolerated. In 1 cycle neutropenia grade III occurred and there was one episode of tachyarrythmia in combination with cardiac failure three weeks after chemotherapy cycle.

In summary, our data show that CLAD is a very promising therapy for patients with multiple myeloma.

1360 PUBLICATION

Clinical significance of p53 protein expression in Non-Hodgkin's lymphoma among Malaysian patients

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In Malaysia as in most developing countries, the majority of non-Hodgkins lymphoma (NHL) are of the aggressive type. Our treatment results with CHOP chemotherapy in aggressive NHL are considerably lower (<40%) than the rates reported from studies conducted in the West.

In this study we have investigated the fequency of p53 protein expression among newly diagnosed Malaysian patients with aggressive NHL and have correlated it with several clinical characteristics including treatment response and survival. Immunohistochemical staining with the p53 monoclonal antibody DO-7 was performed on specimens from 45 patients who were subsequently treated with conventional CHOP chemotherapy.

20 of the 45 lymphomas (45%) had >10% of the cells staining positively for p53. p53 staining correlated with increased LDH and a high IPI score. In addition p53 expression predicted for treatment failure with only 30% of patients with p53 positive tumours achieving a CR versus 55% of patients with p53 negative tumours. p53 expression was also significantly associated with a shorter overall survival.

Our results have shown a high frequency of p53 positive NHL among Malaysian patients and this may in part explain the relatively poor results obtained with CHOP chemotherapy.

1361 PUBLICATION

Long term follow-up of treatment of adult acute lymphoblastic leukemia with two protocols, LALA87 and YUALL. Single center experience

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Objective: 157 adult patients (pts) with acute lymphoblastic leukemia (ALL) of median age 38.1 yrs (range 15–65 yrs) underwent chemotherapy according to protocols LALA87 (112 pts, Group I) and YUALL (EORTC 6861) (45 pts, Group II) between 1989 to 1995. Both protocols include same induction, maintenance and CNS prophylaxis, and only difference is in consolidation with standard doses o drugs in LALA87 (DNR, AraC and L-Asp) and high doses in YUALL (L-Asp, CP and HD-AraC, 1000 mg/m^2/12^h 6 days, followed by VCR).

Results: Complete remission (CR) was achieved in Group I in 76 pts (76% evaluated, 68.2% of all) and in Group II in 31 pt (79.5% evaluated, 67.9% of all pts in the group). The Overall CR rate was 76.9% of all evaluated patients (11.5% died during induction), which comprises 68.2% of all treated patients. The predictive factor for achieving remission was age and FAB subtype. Median duration of CR in Group I was 14 mths and in Group II 11 mths. Median survival of patients achieving CR in Group I was 18 mths and in Group II 13.5 mths. There were no difference in CR rate, DFS and survival between two groups, except significantly better survival in the group of patients with T-ALL, especially Foon II group, but without difference in DFS.

Conclusion: These results are showing that in our two groups of patients there were no difference in overall survival depending on the modalities of consolidation chemotherapy. The long term results of treatment of adult patients with ALL are not satisfactory and need further improvement.

1362 PUBLICATION

ICE protocol as conditioning regimen in autologous bone marrow transplantation in high-grade non-Hodgkin's lymphoma

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Purpose: We report here the results of high dose chemotherapy with ICE (Ifosfamide 3000 mg/m^2 -6 -5 -4 -3, Carboplatin 500 mg/m^2 -6 -5 -4, Etoposide 300 mg/m^2 -6 -5 -4) in a group of high-grade NHL patients (pts).

Methods: We have treated 31 pts from 1993 tom 1997. Clinical characteristics were: female 15, male 16; stage III–IV 18; sistemic symptoms 11; 14 pts had mediastinic bulky disease; 16 were in first complete remission (CR), 5 were in second or third CR, 7 were partial responders and 3 refractory to chemotherapy.

Results: No treatment-related mortality was observed. Nonhematologic toxicity was minimal with 10% of severe mucositis (grade 3 WHO), 2 pts had hepatic toxicity (grade 2 WHO). No other clinically significant toxicities were observed. After a median follow-up of 24 months (range 1–53) overall survival (OS) was 88%. Stage was the only one statistically significant characteristic for OS. After a median follow-up of 21 months (range 1–51) 23 pts were freedom from disease, and disease-free survival (DFS) was 65%. The following characteristics were significantly associated with DFS: presence of bulky disease (93% vs 59% p 0.02), stage I–II (100% vs 55% p 0.004), CR at ABMT (81% vs 60% p 0.007).

Conclusion: We confirm the efficacy of this condictioning regimen and its feasibility in an heterogenic group of patients.

1363 PUBLICATION

Treatment of refractory or early relapsed lymphoma with *MINE* regimen

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Introduction: We report on the activity and tolerance of MINE regimen in patients with refractory or early relapsed intermediate or high grade NHL.

Methods: Seventeen patients, 12 men and 5 women, with refractory or early relapsed intermediate or high grade NHL were entered. The median age was 56 (32 to 75) years. Sixteen (94%) patients were in advanced stage III or IV and 12 (71%) were classified as high grade NHL (WF). According to the IPI, 10 (59%) patients with scores 3–5 were classified as high risk. All patients had been previously treated with either CEOP or CNOP (Novantrone instead of Epirubicin) and for various reasons, were not considered for megatherapy. After this first line treatment, the disease was proven to be resistant in 10 (59%) patients, while in seven patients the disease relapsed in 2–10 months after induced complete remission. The MINE regimen consisted of Mesna 1.33 gr/m^2, Ifosfamide 1.33 gr/m^2, Etoposide 65 mg/m^2 days 1–3, and Mitoxantrone 8 mg/m^2 day 1.

Results: The median number of cycles administered was 5 (2 to 7). Ten (59%) patients responded including 5 (30%) with CR. Four (40%) responders were observed among 10 patients with refractory disease and 6 (85%) among 7 with early relapse. Median survival was 18 months. *Toxicity:* Grade III neutropenia was observed in 10 (59%) patients. All patients exhibited alopecia grade III.

Conclusions: The MINE regimen with an acceptable toxicity is an alternative in the treatment of patients with early relapsed or refractory NHL. Its use may be important in the treatment of patients not eligible for more intensive regimens.

1364 PUBLICATION

Survival and prognostic factors in patients with Hodgkin's disease

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Purpose: The aim of this study is to determine the overall and progression free survival and to evaluate the prognostic factors in patients with HD.

Methods: 125 patients with histologically confirmed HD; treated and followed in our clinic between 1991–98 were evaluated retrospectively

for response to treatment, survival and prognostic factors. Patients were classified into 3 prognostic groups with respect to stage and the presence of risk factors; early stage (I–IIIa) without risk factors (group 1), early stage with risk factors (group 2), advanced stage patients (IIIb–IV; group 3) and treated accordingly.

Results: 27 (21.6%) patients with advanced disease, 56 (44.8%) with early stage and additional risk factors were treated with primary chemotherapy. 71 patients (85.6%) were given standard anthracycline-based combinations. After a median follow-up period of 40 months; 70 (55.6%) patients remain with no evidence of disease and 16 (19.3%) have died. Overall survival (OS) at 7 years in the 1st group was 97.0%; in the 2nd group OS at 5 and 7 years were 81.0% and 60.0%, respectively and that of the 3rd group at 3 years was 80.8%. OS at 5 and 7 years for the whole group were 86.5 and 76.9%, respectively. Progression free survival for the latter group at 5 years was 74.1%. Median survival was not reached in either group. Univariate analysis revealed that ESR > 40 mm/hr (p: 0.0004), age > 50 years (p: 0.0001) and the presence of risk factors (p: 0.0089) were associated with a poor prognosis. Age > 50 years and ESR > 40 mm/hr were also shown to be independent prognostic factors by multivariate analysis.

Conclusion: ESR > 40 mm/hr and age > 50 years are major prognostic factors with an adverse effect on the outcome of patients with HD.

1365 PUBLICATION

Drug resistance mechanisms in EBV-associated multiple myeloma as posttransplantation lymphoproliferative disorder

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The posttransplantation lymphoproliferative disorders (PT-LPD) are Epstein-Barr virus driven diseases. Multiple myeloma as PT-LPD is rare. Since complete response to chemotherapy has not been published in this disease, expression of drug resistance mechanisms are probable but have not been evaluated yet. We determined the expression of mRNAs encoding classical and atypical MDR-associated factors by RT-PCR. The cells were monoclonal, showed a high proliferative activity, expressed BB4 but not CD 20. P-glycoprotein and cMOAT were strongly overexpressed. In addition, H19 and NCA expression was increased. No modulation of the expression of LRP, Topo IIα, Topo IIβ, MLH1, MSH2 and MXR7 could be observed. These results might might give us some insight into the drug resistance features of EBV-associated multiple myeloma cells occurring as PT-LPD.

1366 PUBLICATION

Evaluation of drug resistance mechanisms in mast cell leukemia

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Malignant mastocytosis and mast cell leukemia are rare forms of mastocytosis characterized by uncontrolled proliferation of mast cells in diverse organs. No effective therapy is known although some patients may benefit from interferon and corticosteroid treatment. Drug resistance mechanisms in this disease have not yet been evaluated. We determined the expression of mRNAs encoding classical and atypical MDR-associated factors by RT-PCR in human malignant mast cells. P-glycoprotein was strongly overexpressed. MRP, LRP, cMOAT, H19 and NCA were also overexpressed. No modulation of the expression of Topo IIα, Topo IIβ, MSH2 and MXR7 could be observed. Dexamethason had an inhibitory effect at 1 μg/mL on colony formation. No inhibition of colony formation was detected with cytosine arabinoside at 1 μg/mL and interferon alpha at 10 IU/mL but at higher concentrations with these drugs. These results might give us some insight into the drug resistance features of human malignant mast cells.

1367 PUBLICATION

Cancer and radiation therapy in Behçet's disease

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Introduction: Behçet's disease is rarely reported in association with malignancies. No data about radiation therapy morbidity in the presence of Behçet's disease is reported. Here, seven cases of Behçet's disease concurrent with malignancy and morbidity of the radiation therapy are reported.

Patients: Several malignancies were diagnosed in seven patients with the history of Behçet's disease at Hacettepe University Faculty of Medicine between 1987 and 1998. Median age at the diagnosis of malignancy was 44 (25–55) years. The malignancies were cervix, bladder, stomach, pancreas cancers, malignant mesenchymal tumor, Hodgkin and non-Hodgkin lymphomas. Four patients received radiation therapy as primary or adjuvant therapy in conventional fractionation and conventional total dose. Three of them experienced severe late radiation reactions of brachial plexopathy, ureter fibrosis and skin necrosis 4 to 6 months after termination of radiotherapy.

Conclusion: Lymphoma and leukemia have been reported previously in the literature in association with Behçet's disease and cytotoxic agents used in the treatment of this disease were accused to be the causative factors. Solid tumors may also be observed in the course of Behçet's disease as it is the case in the present report. We assume that vasculitis which is a known basic histopathological mechanism in Behçet's disease may have played a role in the development of severe late radiotherapy morbidity.

1368 PUBLICATION

Hepatitis c virus infection (HCV) and b-cell non-Hodgkin lymphoma (NHL)

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We designed the present study to investigate the prevalence of this association among Spanish B-cell NLH patients and correlate virological findings with clinical features.

Methods: In this transversal study, between January 1998 and December 1998, 52 lymphoma patients were recruited. All patients had received prior chemotherapy or they were under treatment. Patients with prior history of intravenous drugs abuse or human immunodeficiency virus were excluded. Patients were classified according to Working Formulation and the Ann Arbor system. Sex, 27 were men and 35 women; the mean age was 54.9 years (20–76). Low grade lymphomas 23, intermediate 13, high grade 16. All patients were tested by antibodies and HCV RNA presence. Serum virus C antibodies were examined by ELISA and Immunoblot. RNA virus was analyzed by RT-PCR. Positive samples underwent genotype identification by line probe assays.

Results: We detected HCV in 6 patients (11.53%) with no discordance between both techniques in any case. Genotype was determined in 4/6 cases, and 1b (Simmonds classification) was detected in all of them. Histological type: 2/6 low grade, 1/6 intermediate and 1/6 high grade lymphoma. Among the six positive C virus patients, 5 had increased transaminasemia.. Clinical complete response of the HVC(+) B-cell NLH was achieved in 4/6 and in 21/46 of HVC(−)

Conclusions: Spanish patients with B-cell NHL exhibited a HCV prevalence of 11.53%. The predominant HCV genotype was 1b No significant difference in clinical response was observed.

1369 PUBLICATION

Management of primary Non-Hodgkin's lymphoma (PNHL) of the liver: Our experience

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Purpose: PNHL of the liver represents a singular and rare tumor with few clinical eases reported in literature (about 100) and a peculiar location (0.4% of all extranodal sites). The purpose of this short report was to define the