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

correct management of this neoplasia with the help of two clinical cases observed in the last four years.

Methods: 2 young females of 32 and 39 years old were admitted to our Dept. in 1994 and 1997 respectively. The patients (pts) complained diffuse abdominal pain, nausea, anorexia and weight loss. The clinical examination underlined the absence of palpable masses and presence of hepatomegaly. Laboratory findings emphasized the following results: increased LDH > 700 U/L, γGT > 50 U/L, alkaline phosphatase > 250 U/L, VES > 50, HCV-RNA$^+$ with normal values of CEA and αFP. The thoracic and abdominal CT scan showed hypodense and diffuse masses of the liver in boht pts. Finally, by means of an hepatic FNAB, the exact diagnosis was carried out. So, 8 cycles of CHOP chemotherapy were administered. Then, at the end of the scheduled cycles, pts received α-2b Interferon (3 m.I.U.) 3 times at week for 6 consecutive months.

Results: An intensive follow-up consisted of clinical and laboratory exams every 3 months, hepatic US and/or CT abdominal scan every 6 months was established. After a follow-up of 36 months and 12 months respectively, pts are alive with no evidence of disease (100% CR).

Conclusion: this short report confirmed the importance of hepatic FNAB to achieve the correct diagnosis and showed that the adopted CHOP plus α-2b Interferon chemotherapy was effective and well tolerated.

1370 PUBLICATION

Retrospective evaluation of the risk profile in chronic myelogenous leukemia (CML) according to a new prognostic scoring system

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Several prognostic scoring systems have attempted to identify the risk factors for the predictions of overall survival at diagnosis of CML. Until recently, the most widely accepted was Socal's risk index, however, a new scoring system has been proposed in 1998 for patients treated with interferon alpha (IFN-a) (Hasford et al, J Natl Cancer Inst, 90: 850). This system takes into account age, spleen size, percentage of peripheral blasts, eosinophils, basophils and platelet number. We undertook a retrospective analysis of a series of 71 Ph positive CML patients according to the new risk scoring system. Patients were stratified in low, intermediate and high risk group (n = 19, 16 and 36, respectively) with median overall survival of 92, 52 and 46.5 months respectively. In order to evaluate the predictive value of the new risk scoring system, we performed a univariate analysis so as to identify statistically significant associations between risk score and survival. Although the number of patients included in this analysis is not very large, a statistically significant association was found between low risk score and longer overall survival ($p < 0.02$). Furthermore, in the low- and high-risk groups, treatment with IFN-a was significantly associated with better outcome ($p < 0.04$ and <0.006, respectively) compared to other forms of treatment (hydroxyurea, alkylating agents). In all three risk groups, the type of bcr-abl chimeric transcript (b_3a_2 v b_2a_2) did not seem to affect prognosis. In conclusion, our analysis generally confirms that the new scoring system offers a reliable means for the estimation of overall survival in CML; however, it should be noted that its predictive value was more limited in the intermediate risk group. If the same results are repeated in further studies with larger number of patients, the new scoring system could be of special help for the application of risk-adjusted therapies and the identification of patients most likely to benefit from bone marrow transplantation.

1371 PUBLICATION

Therapy of Morbus Hodgkin in one Pediatric Oncohaematologic Center in Ukraine

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Purpose: Modern Chemotherapy-Radiotherapy Strategy for treatment childrens and adolescents with Morbus Hodgkin was introduced to improve outcome for these patients.

Methods: Therapeutical Germ Protocol DAL-HD-90 was used in Pediatric Oncohaematologic Department in Kiev Regional Oncologic Dispensary for treatment of 34 patients (23 boys and 11 girls, median age 10 y 5 m with range 4 y–18 y 4 m) with initially diagnosed Morbus Hodgkin: Stage IIA was in 11, IIB-4, IIIA-8, IIIB-3, IVA-2, IVB-in 6 pts.

Results: 5-years pEFS for total group was 0.80 (SD = 0.1); 1 pt was NR, 4 pts relapsed, nobody died because of therapy complications.

Conclusions: Therapy results became dramatically better after introducing of modern principles in diagnosis and therapy. For further improvement of patients, outcome mare accurate stratification and more detailed investigations are needed.

1372 PUBLICATION

Induction of apoptosis by new alkylphosphocholines

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The aim of the study was to investigate the cytotoxic effects of erucylphosphocholine (EPC), erucylphospho-N,N,N-trimethylpropanolamine (EPC3) and octadecyl-(1,1-dimethylpiperidino-4-yl)-phosphate (ODPP) on human leukemic cell lines with (K-562, LAMA-84, BV-173 and CML-T1) or without (HL-60, THP-1, TMM, SKW-3 and EB-1) expression of BCR-ABL. EPC, EPC3 and ODPP showed relatively low IC50 values in BCR-ABL negative cells (about 5 μM). However, all BCR-ABL positive cell lines were resistant (IC50 > 20 μM). Following an incubation of 24 h, the APC caused oligonucleosomal DNA fragmentation typical for programmed cell death in HL60, SKW-3 and THP-1 cells. BCR-ABL positive cells, however, showed an apoptotic DNA ladder only after prolonged incubation (48 h) and following higher concentrations of the test compounds. Induction of apoptosis was confirmed by ELISA. Experiments with a cell-free system consisting of cytosolic fraction from treated and nuclei from untreated cells showed that DNA fragmentation was caused by cytosolic extracts from HL-60 and SKW-3 cells exposed to EPC in nuclei from K-562, LAMA-84 and SKW-3 cells. Thus, the induction of apoptosis is a common mechanism of the anti-leukemic activity of alkylphosphocholines. We suppose that expression of BCR-ABL is the main cause for the retarded apoptosis and resistance observed.

1373 PUBLICATION

Beta-2-microglobulin elevated serum levels highly correlate with tumor burden and clinical response in newly diagnosed and relapsed Non-Hodgkin's Lymphomas treated with standard doses chemotherapy

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The role of beta-2-microglobulin as a prognostic factor in Non-Hodgkin's Lymphomas (NHLs) has been emphasized by many authors. We analyzed beta-2-microglobulin (beta-2-m) serum levels of 74 consecutive patients (PTS) affected by newly-diagnosed or relapsed low-grade (31) or intermediate-high grade (43) NHLS. All the patients have been treated with standard doses chemotherapy. Thirty PTS (40.5%) showed beta-2-m serum levels higher than 3 mg/L that we considered as the cut-off value. We analyzed the main prognostic factors of beta-2-m-positive (beta-2-m+) PTS according to the International Prognostic Index (I.P.I.) and compared them with those expressed by beta-2-m-negative (beta-2-m−) ones. Beta-2-m serum levels showed a high correlation with elevated LDH serum levels ($p = 0.03$) and stage according to Ann Arbor Classification ($p = 0.0001$), two clinical features currently used as markers of the tumor burden. The complete clinical remission (CCR) reached with standard front-line chemotherapy also correlates with the presence of normal serum levels of beta-2-m.

No correlation were found between beta-2-m serum levels and the others prognostic factors: age ($p = 0.54$), Performance Status ($p = 0.078$), extra-nodal sites of disease ($p = 0.1$), I.P.I. subgroups ($p = 0.45$). In conclusion, our data confirm that beta-2-m serum levels may play a role as a measurable marker of tumor burden and as a prognostic factor in NHLs.

1374 PUBLICATION

Low dose Idarubicine, Vincristin, Prednisone, and G-CSF plus ATRA for the treatmant of poor risk myelodysplastic syndrome (MDS)

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Purpose: The myelodysplastic syndromes (MDS) are heterogenous group of disorders with an invariably fatal outcome. Other than bone marrow transplantation, no treatment has been able to alter the natural history of MDS. Many of the drugs that have been evaluated in attempt to increase