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

remissions and prolong survival. We examined the clinical results of low dose Idarubicine, Vincristin, Prednisone, and G-CSF plus ATRA in patients with poor risk MDS.

Methods: Six patient [subgroups were RAEB (n = 2), RAEBt (n = 2), CMML (n = 2)] received Idarubicine 5 mg/m^2/week, Vincristine 1 mg/m^2/week, Prednisone 1 mg/kg/day for four week. G-CSF (5 μg/kg/day) was given on days 2–6, 9–13, 16–20 days. The dose of G-CSF was adjusted to normalize the ANC if the pre-treatment ANC value was less than 1.500/ml, or to double the ANC if above 1.500/ml. ATRA (25 mg/kg/day) was started at 29th day of treatment. The minimum follow-up duration of all patients was 12 weeks.

Results: Among six patients (therapy for at least 12 weeks), two patients showed no response while four patients showed hematopoietic responses. Of four responding patients, three had tri-lineage responses, one had bi-lineage responses. All responding patients showed at least % 50 reduction in red cells requirements and % 80 reduction in platelets requirements.

Conclusion: We concluded that low dose Idarubicine, Vincristine, Prednisone, and G-CSF plus ATRA combination regimen is effective in improving the cytopenias in MDS and deserves further investigation.

1375 PUBLICATION

Results of primary irradiation in non-Hodgkin lymphoma stage I and II and analysis of recurrences

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Purpose: Evaluation of primary irradiation in stage I and II non-Hodgkin lymphoma, definition of subgroups and analysis of recurrencies.

Methods: 87 patients (47 male, 40 female) median age 63 yrs. underwent primary irradiation due to NHL stage I (n = 60) and II (n = 27). Low grade was presented in 36 patients (pat.) and high grade in 51 pat. A nodal involvement showed 58 pat. and an extranodal involvement 29 pat. A supradiaphragmal localisation occurred in 65 pat. and infradiaphragmal in 17 pat. A median dose of 40 Gy was delivered (single fraction 1*–2 Gy; *twice a day). Recurrence occurred in 41 pat at 9.2 mort (median) after treatment in 28 pat. stage I and 13 pat. stage II, with in field and border n = 8 only.

Results: Overall survival at 5 and 10 yrs (yr-sr) was 69% and 52% with a better survival of male pat. at 10 yrs (59% vs. 43%). No significant difference was seen comparing stage I and stage II (72% and 51% vs. 65% and 50.3%; 5 and 10 yr-sr). Patients with extranodal involvement survive signifivant better than pat. with nodal involvment (86% and 69% vs. 59% and 44%; 5 and 10 yr-sr; p = 0.0082). We also observed better survival in younger pat. <63 yrs. There was no influence of irradiation dose </> 40 Gy. Pat. with a recurrence >9.2 mon. had significant better survival compared to pat. <9.2 mon. (67% and 45% vs. 42% and 23%; 5 and 10 yr-sr; p = 0.026). In treating recurrence a complete remission could be achieved in 13 pat. showing benefit in combining irradiation and chemotherapy.

Conclusion: Irradiation alone is sufficient to control early stage NHL with a better outcome of extranodal presentation. The high rate of recurrences depends mostly on insufficient staging. Recurrences should be treated with chemotherapy and irradiation.

Urological malignancies

1376 ORAL

Outcome following high dose rate (HDR) brachytherapy (BT) and external beam radiation for localized prostate cancer

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Purpose: To evaluate a new interdisciplinary therapy protocol for survival, morbidity and prognostic variables for men with prostate cancer.

Material and Methods: The files of 189 men aged in median 69 years (44–84) receiving curatively intended combined high dose rate (HDR) 192 Iridium-brachytherapy (BT) and external beam radiation (EBR) for localized prostate cancer were recorded prospectively. Hundred and twenty-seven patients had T1–2 tumors, and 62 patients had T3 tumors. The total planned dose applied by external beam radiation was 50 Gy in the small pelvis, and 40 Gy in the prostate by in-field-dose modification. The HDR-brachytherapy was delivered in two fractions. The dose per fraction was 15 Gy for the target.

Results: Mean survival was 6 years (range 12–143 months), 76.7% of the patients survived and 86.3% were disease-free. The biochemical non-evidence of disease rate (bNED) was 78%. Univariate survival analysis revealed that low stage (T1–2), low grade (G1–2), normal PSA status after radiation therapy, and no adjuvant hormonal treatment were associated with long survival. However, the stratification for adjuvant hormonal treatment was not according to random. In multivariate analyses PSA status was the only independent prognostic factor in terms of survival.

Conclusion: The results confirm that HDR-BT combined with EBR is curative and especially effective in high risk cases of localized prostate cancer.

1377 ORAL

Conformal proton therapy for prostate carcinoma

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Purpose: Evaluate the role and optimal dose of radiation therapy required to eradicate prostate cancer utilizing conformal proton beams to deliver precision therapy.

Methods: 643 patients with localized prostate cancer were treated with protons. The patients received 74 to 75 CGE (Cobalt Gray Equivalent) at 1.8 to 2.0 CGE per fractions. The patients were evaluated for response to therapy and treatment related toxicity.

Results: Overall biochemical disease-free survival rate was 79% at five years. The rate was dependent upon both the initial PSA and the post-treatment PSA nadir, with patients who had an initial PSA of <4.0 ng/ml and those with nadirs <0.51 ng/ml having five year biochemical disease-free survival rates of 89% and 91% respectively. Minimal radiation proctitis was seen 21% of patients; toxicity of greater severity was seen in less than 1% of patients.

Conclusion: Conformal proton therapy to 74–75 CGE produced minimal treatment related toxicity and excellent PSA normalization and disease-free survival in patients with low initial PSA levels.

1378 ORAL

Effect of neoadjuvant (Short Course) LHRH analogue treatment with radical radiotherapy on long term hormonal status of patients with localised prostate cancer

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Introduction: Neoadjuvant hormone cytoreduction before local radiotherapy has been shown to improve tumour control in three phase III trials and has been adopted as a standard treatment for localised prostate cancer by many centres. However, the issue of long term endocrine effects of this treatment has not been adequately addressed.

Patients and Methods: We have evaluated the endocrine effects of short-term neaoadjuvant LHRH agonist administration (mean number of monthly depot injections: 3.7 months) followed by radical radiotherapy in 419 patients with localised prostate cancer treated between 1989 and 1997. We analysed levels of serum testosterone (n = 852), LH (n = 799) and FSH (n = 801) at four phases of management, prehormone (PH), on hormone therapy (OT), within 26 weeks after completing therapy (R) and on long term follow-up (F) (median: 54 weeks).

Results: Suppression of pituitary gonadotropins and testosterone following administration LHRH agonist and their recovery after cessation of the drug was clearly observed. When comparing PH and F levels median serum testosterone levels decreased from 16 nmol/l to 14 nmol/l (p = 0.018), median serum LH increased from 5 U/l to 8 U/l (p < 0.0001) and median serum FSH levels increased from 6 U/l to 20 U/l (p < 0.0001). Serum testosterone levels returned to within the normal range in 91.2% of patients with a compensatory rise in serum levels of luteinizing hormone.

Conclusion: Our data suggest a minor degree of residual gonadal dysfunction after short-term administration of LHRH agonists and radical radiotherapy. Further evaluation of testicular radiation dose will allow an estimate of the effects of each component of combined modality treatment.