190

SECOND SOLID TUMORS IN HODGKIN DISEASE: OUR EXPERIENCE

Addamo GF., Sogno G., Pastorino G., Martini MC. Vallauri M., Moraglio L., and Brema F.,
Department of Medical Oncology, S. Paolo Hospital, Savona, (Italy).

Combined chemo-radiotherapy in Hodgkin disease (HD) obtained a significative increase of survival and recovery rate. An increase of relative risk of second tumors was observed in those patients (pts) successfully treated for HD. In 3/21 pts treated for HD from 12/85 to 6/93 we observed a second solid tumor: 2 non small cells lung cancer (epidermoids) and 1 pleural malignant mesothelioma, 13, 20 and 45 months after HD diagnosis, respectively. All these 3 pts received, for HD treatment, radiotherapy: mantle field irradiation in 2 pts and involved fields (mediastinum) irradiation in 1 pt. Two pts also received concomitant polichemotherapy (COPP/ABVD 3/3 courses and ABVD 3 courses); thirds pt received 3/3 courses of COPP/ABVD for relapsing disease. The short latency of the second tumor suggests a possible role of HD patients' immunodepression instead of strictly iatrogenous pathogenesis. These observations induce to alert and prolonged follow-up in the patients treated with success for HD.

191

RESULTS OF CHEMOTHERAPY COMBINED WITH INVOLVED -FIELD RADIOTHERAPY/IF-RT/ FOR CHILDHOOD HODGKIN'S DISEASE /HD/

W.Balwierz
Dep.Hemat.,Children's Hospital Collegium Med. Jagiellonian University,Krakow, Poland

In the years 1970 to 1987, 125 children with HD /stages I-IV/were treated with MVPP and/or B-DOPA combined with IF-RT.The intensity of therapy was gradually adjusted to the stage of HD. Along with a modified therapy protocol 2 consecutive periods of time were analysed.The effect of 17 various factors on the relapse free survival/RFS/by multivariate analisis were tested. The 10-year RFS rates were 80% for first period /1970 to 1979/and 92% for second one,respectively.We received better results and decreased of serious complications in the second than in the first period.Of 17 variables tested,the number anatomical regions involved and total tumor burden were independent indicators for RFS. Multidrug chemotherapy combined with IF-RT seems now to be optimal method of treatment of HD. Intensity of therapy should be tailored to the extent of disease.

192

PRIMARY CUTANEOUS B-CELL LYMPHOMA (CBCL).

Bari M., Segati R., Azzarello G., Sampognaro E., Rosetti F., Pappagallo G.L., Manconi R. ,Lodi P. L. and Vinante O. - C.O.M. ULSS 17, Noale VE, Italy.

From 1988 to date 5 cases of CBCL were observed, aged from 50 to 81 years, 4 diffuse-centroblastic (DC), and 1 nodular-centroblastic-centrocytic (NCC) at immuno-histochemistry. CT scans, laparoscopy, and biopsies excluded for extra-skin localizations. The NCC, CBCL lesion appeared 10 years ago in the back skin of a 54 year male, being alternated with spontaneous remissions. One out of 4 DC, CBCL lesions was in the back skin of a 50 year male; the patient has come to the Oncologist's observation 4 years later, presenting a lesion of 20 x 27 cm.; by combining MACOP-B chemotherapy and radiation, a complete remission (CR) lasting 2 years was obtained. The 2nd DC, CBCL appeared as a 3 cm. diameter lesion in the back skin of a 62 year female; after 5 months (3 before, and 2 after diagnosis) the primary increased to 6 cm., and new lesions were observed as cutaneous nodes, without l.n. spread; VCMP chemotherapy was administered, with a CR lasting 8 months. The 3rd DC, CBCL patient was a 81 year male with the primary lesion spreading to all the pubes skin; VP16 plus mitoxantrone obtained no response. The last DC, CBCL was observed in a 64 year male as a 2 cm. diameter lesion in the scalp; after surgery, the patient is free from neoplastic disease at 6 months.

Conclusions: CBCLs in this series maintained a long-lasting skin-homing, demonstrating local aggressiveness, and in our opinion they may be considered as non-low-risk lymphomas. The achievement of local control of disease may improve prognosis.

193

ProMICE-CytaBOM CHEMOTHERAPY IN AGGRESSIVE NHL. A PRELIMINARY REPORT

Caracciolo F., Petrini M., Capochiani E., Papineschi F., Casalino F., Grassi B.
Heamtology Unit - S. Chiara Hospital - University of Pisa - Italy

Between December 1991 and December 1993, 21 patients with aggressive non-Hodgkin lymphomas, previously untreated, were entered in this study. The regimen consisted of idarubicin 8-12 mg/m^2 iv bolus on day 1, VP-16 120 mg/m^2 in a 60-minutes iv infusion on day 1, CTX 650 mg/m^2 in bolus on day 1, PREDN 60 mg/m^2 po on days 1 through 14; ARA-C 300 mg/m^2 iv bolus on day 8, BLEO 5 mg/m^2 iv bolus on day 8, VCR 1.4 mg/m^2 iv bolus on day 8, MTX 120 mg/m^2 iv bolus (with leucovorin rescue) on day 8. The next cycle begins on day 29. The dosage of idarubicin has been 8 mg/m^2 for 3 patients, 10 mg/m^2 for 2 patients, and 12 mg/m^2 for 16 patients. Median age was 51 years (ranging from 30 to 58). Nine patients were female, 15 had B symptoms, 12 presented bulky disease, and 3 presented bone marrow involvement. Four patients were histologically low-grade lymphomas but were treated with this schedule for aggressive clinical picture. All patients were treated on an outpatient basis. Of the 18 evaluable patients 8/18 achieved a complete remission, 6/18 a partial remission and 4/18 patients were considered non responders. Toxicity was very mild, with only 3 patients experiencing grade III-IV mielosuppression. 4/6 patients who achieved PR were low-grade lymphomas.

Median follow-up is 10 months. Four patients have relapsed at +2, +3, +10, +11 months. In our experience the introduction of idarubicin in a ProMICE-CytaBOM derived regimen showed a satisfactory rate of CR, and a very mild toxicity even with the higher dosage of idarubicin. The negligible toxicity observed may suggest to shorten the intercycle period (from 28 to 21 days) in a larger series of patients.

194

Extracutaneous clonal TcR-Beta rearrangement on cutaneous T-cell lymphoma (CTCL) and T-Pseudolymphomas (PSL).

S.N.W.Dommann*, C.C.Dommann-Scherrer**, D.Zimmermann**, M.T.Zimmermann-Dours**, E.Kung*, G.Burg*..Departments of Dermatology* and Pathology**, University Hospital, Zurich, Switzerland.

Extracutaneous involvement is a poor prognostic sign in cutaneousT-cell lymphomas (CTCL); however its clinical or histological manifestation gets evident usually only late in the course of the disease.It was the purpose of our study to prove with genotypic analysis extracutaneous involvement (peripheral blood, lymph node and bone marrow) at times, when extracutaneous involvement cannot be demonstrated on a macro- or micromorphologic level. A total of 25 patients (5 Mycosis fungoides, (MF); 4 Noh-MF CTCL; 7 Sézary syndrome, (SS); 8 T-Pseudolymphoma, (PSL) and 1 Lympho-matoid papulosis) were investigated. Genotypic analysis of these specimens were performed by non-radioactive Southern blot analysis using digoxigenin-labelled c-beta (TcR-Beta) and J heavy (JgH) probes on DNA extracted from fresh frozen material. Clonal rearrangements were confirmed for each gene locus in two independant restriction enzyme digests. The numbers of probes showing clonal rearrangement for TcR-Beta chain gene are given in the following table. These results indicate an early systemic spread of neoplastic cells in CTCL.

Diagnosis	Number	Skin*	Lymph node*	blood*	bone marrow
LP	1	0/1	nd	nd	nd
PSL	8	0/8	nd	0/2	nd
Non-MF CTCL	4	2/4	nd	0/2	1/1
MF	5	3/4	2/2	1/2	nd
Sézary S.	7	7/7	6/6	6/6	1/1

* clonal rearrangement/number of probes studied. nd=not done

195

Epidemiological, virological and clinico-pathological data from 114 patients (pts) with Hodgkin's disease and HIV infection (HD-HIV):

D. Ernste, U. Tirelli, D. Serraino, S. Franceschi, M. Boiocchi, E. Vaccher, A. Carbone for the GICAT (Italian Cooperative Study Group on AIDS and Tumors), C.R.O. Aviano - Italy.

Since November 1986, 114 cases (103 m, 11 f) of HD-HIV have been collected by the GICAT. The median age was 29 years (19-57), 80% were IVDU in accordance to the overall epidemiology of HIV infection in Italy. At the diagnosis of HD, 17% of pts had AIDS, 22% ARC, 29% PGL and 34% were asymptomatic; median CD4+ cell count was 275/mm^3 (9-1100). Lymphocite predominance (LP) was observed in 4%, nodular sclerosis (NS) in 30%, MC in 44% and LD in 21% of pts. In comparison with 125 Italian HD pts not infected with HIV, observed in the same period of time at our Institution and with a comparable median age, a 4-fold higher frequency of the MC and an approximately 12-fold higher frequency of the LD subtypes were detected among pts with HD-HIV.

To determine whether EBV may play a role in HD-HIV we characterized EBV (latent membeane protein, LMP-1) in HD samples from 18 pts with HD-HIV as well as from a control population of 104 pts with HD. EBV was detected in 14/18 (78%) HD samples from the former group, but only in 27/104 (25%) HD samples from the latter group ($p < 0.001$) indicating that EBV may be more pathogenetically involved in HD-HIV, as previously reported for HIV-associated NHLs.

Thirty-one/108 (28%) and 56/108 (51%) pts were stage III and IV respectively; 78% of pts had B symptoms. These figures were significantly different from those observed in pts with HD of the general population. Twelve pts received no treatment, 7 pts radiotherpy (RT) alone, 53 pts were treated with standard CT (MOPP, MOPP-/ ABVD ± RT) and obtained 45% complete remission (CR) and 34% partial remission (PR). Twenty six pts were treated prospectively with EBV ± P (Epirubicin, Bleomycin, Vinblastine ± Prednisone) + AZT ± G-CSF and obtained 58% CR and 27% PR.

The median survival of all pts was 15.3 months. Pts with CD4 + lymphocites ≤ 250/mm^3 at onset of HD had a median survival of 11.5 months, while those with CD4+ > 250/mm^3 a median of 38 months ($p = 0.002$). The median survival of pts without and with AIDS at onset of HD was 27 months and 9 months respectively ($p < 0.001$) and for pts achieving or not CR was 11 months and 58 months respectively ($p < 0.001$). Pts without B symptoms survived significantly longer than pts with B symptoms (43 vs 12 months, $P < 0.001$). Age more or less than 30 years, sex, risk group (IVDU vs other groups), stage (I + II vs III + IV), extranodal involvement, were not factors influencing survival. The median survival of 26 pts treated with EBV ± P + AZT ± G-CFS was not different (13 months) from that of pts treated with standard CT (17 months) but a statistically significant lower rate of opportunistic infections (OI) occurred in the first group (32% vs 74%, $p = 0.003$) during or after treatment. In conclusion, in comparison to HIV-negative HD there is evidence of a significant increase of: 1) MC and LD subtypes, 2) EBV expression in tumor tissue. Moreover, there is evidence of feasibility of antiretroviral therapy and CT with a significant reduction of OI. Supported by grants of AIRC.