935

SECOND MALIGNANT NEOPLASMS IN PATIENTS WITH HODGKIN'S DISEASE

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Of 478 patients treated for Hodgkin's disease (HD) from 1954 to 1987 at the University of Rochester Cancer Center, 97% could be evaluated for the risk and characteristics of SMN. Comparisons were made with observed-to-expected incidence ratios (OER's) using age and sex-adjusted rates from the NCI SEER data for 1973-1988. 48 patients developed a SMN for a crude incidence of 10% (OER=4.47). In patients that received any XRT, 75% of the SMN occurred within or <2cm from the radiation portal. The mean interval from the diagnosis of HD to SMN was 11.9 years. The median survival for the entire HD population was 22.1 years, and following diagnosis of SMN it was 1.5 years. Leukemias occurred in 7 patients (14.6%), and solid tumors in 40 (83.3%). There was no association between the occurrence of leukemia, and laparotomy with splenectomy. The most significant finding is as follows: despite the progressively increasing incidence of SMN with duration of F/U, the OER did not change with time due to a similar increase in the expected incidence of cancer in people without HD.

936

SECOND MALIGNANT TUMORS (ST) AFTER TREATMENT FOR HODGKIN'S DISEASE (HD)

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A not negligible proportion of the patients (pts) cured of HD will succumb to a ST. We analyzed retrospectively ST occurrence in 1021 pts with HD treated in Florence until 1988 and compared our results with those of the literature. Seventy-two of them presented a ST: a second solid tumor (SST) in 62, acute leukemia (AL) in 10. To better elucidate the possible link between ST occurrence and the treatment given for HD, actuarial cumulative incidence was separately calculated both for the 50 ST ocurring during the relapse free period (considering pts who experienced a relapse as censored at the date of relapse) - *first study* - and for the 22 ST occurring after relapse -*second study*- In the *first study*, actuarial 10-yrs ST, SST and AL incidence resulted to be 5,1%, 4,3%, 0,9% respectively. Corresponding values for 20 yrs incidence are 18,5%, 17,5% and 1,4%. AL incidence seems to plateau after 10-15 yrs, while that of SST continues to rise with time. On the whole, actuarial 10 yrs ST incidence is higher in pts aged > 41 when HD was diagnosed (12%) than in the younger ones (3%) and in those treated with radiochemotherapy (RT + CT, 7%) or chemotherapy (CT, 9%), as opposed to pts treated with radiotherapy alone (RT, 4%). These differences are significant. Although the number of events is small, AL actuarial 20 yrs incidence is significantly higher in pts treated with CT (3%) or RT+CT (11%) than in those treated with RT alone (0.2%). A trend is evident toward an higher incidence of AL among pts treated with MOPP as opposed to ABVD (5% vs0% at 20 yrs) or with more than 6 cycles of CT (9% vs 2% at 20 yrs). In the *second study*, ST incidence was analyzed according to primary and salvage treatment and to other clinical factors. Again, the most relevant differences in ST distribution were observed according to age at diagnosis of HD.

Keywords: - second malignancies; - Hodgkin's disease; pathogenic damage.

937

EARLY STAGES OF HODGKIN'S DISEASE TREATED WITH A DECREASED DOSE OF RADIOTHERAPY : PROGNOSTIC VALUE OF BETA$_2$-MICROGLOBULIN. Tortochaux J., Fleury J., Dionet C., Chollet Ph. Centre Jean Perrin, 58 rue Montalembert, 63011 Clermont-Ferrand Cedex 1, France.

From 1973 to 1989, the treatment of early stages of Hodgkin's disease (I to III A) in our institution has been characterized by decreasing the dose of radiotherapy delivered, with respect to the irradiated areas described by H.S. Kaplan.

All patients (n = 107) have been treated by initial chemotherapy followed by radiotherapy ; the treatment was ended by chemotherapy in case of poor prognostic factors. The mean dose delivered at mid-mediastinum has so been reduced from 41 Gy to 35 Gy.

Overall survival and disease-free survival have not been altered by such a policy ; complications also did not significantly differ, excepted the lower outcome of herpes zoster.

In our series, conventional factors such as anatomic stage, A or B symptoms, histologic type, erythrocyte sedimentation rate did not present any prognostic value ; so we have introduced in initial staging the beta$_2$-microglobulin plasma level determination, which appears to be an important predictive item with regard to the overall survival.

In conclusion, we assume that the mean dose could usually reach 35 Gy ; furthermore a confirmation that the beta$_2$-microglobulin level could play an important role as a predictive factor would lead to avoid a dramatic lightening of therapy.

938

THE TREATMENT OF CLINICAL STAGES I AND II HODGKIN'S DISEASE WITH A SPECIFICALLY TAILORED THERAPY ACCORDING TO PROGNOSTIC FACTORS

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Controversy still exists over the optimal management of early-stage Hodgkin's disease (ESHD). From 1989 to 1991 we treated 30 non-laparotomized patients (pts) with supradiaphragmatic ESHD (median age 35y, range 16-79y; M/F=14/16; clinical stage I/II=5/25) according to presenting features. Nineteen pts with one or more of the following prognostic factors were defined as unfavourable group (UG): age>50, "B" symptoms, bulky disease, >4 involved sites, "E" lesions, ESR>50 and lymphocyte depleted histology. They received 6 cycles of MOPP/ABV hybrid chemotherapy (M/A) combined with mantle field irradiation. Ten pts with no adverse features were defined as favourable group, and were treated by subtotal nodal irradiation (6 pts) or 4 cycles pf M/A in combination with irradiation to the mantle field (4 pts). One patient had a very favourable presentation of stage I high cervical lymphocyte predominant disease, and received mantle field irradiation alone. Pts have been followed for a median of 26 months (range, 11 to 45 months). They all achieved a complete remission, and they are all alive. One UG patient has recently relapsed and is currently under salvage therapy. In conclusion, a policy of treatment selection based upon initial prognostic factors may achieve excellent results in clinical stages I and II Hodgkin's disease.

939

EVALUATION OF PROGNOSTIC FACTORS IN HODGKIN'S DISEASE

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A total of 212 previously untreated patients with Hodgkin's disease (HD) were consecutively submitted to radiotherapy with or without chemotherapy according to a protocol followed from 1977 till 1985.

The five year disease free survival rates by clinical stages (CS) were 91.5% for CS I, 72.7% for CS II$_A$, 54% for CS II$_B$, 71.7% for CS III$_A$, 25% for CS III$_B$ and 19% for CS IV. Relapses occurred in 4.3% of previously involved irradiated areas.

Results were submitted to statistical analysis for different factors such as: age, sex, number or volume of involved lymphatic areas, mediastinum presentation, systemic symptoms, ESR and histologic subtypes.

Treatment complications were acceptable with herpes zoster in 9.3%, sternoclavicular atrophy in 4.6%, caries in 1.4%, pneumonia in 1.8%, esophagytis in 0.5% and medular aplasia in 0.9%.

In 7 patients (3.3%), Hodgkin's disease was associated with a second malignancy that appeared in six cases 1 to 5 years after combination of radiotherapy with chemotherapy and in one patient, 2 years after radiotherapy alone.

940

HODGKIN'S DISEASE: A STUDY OF PROGNOSTIC FACTORS IN A GROUP OF 308 PATIENTS TREATED AT A SINGLE CENTRE.

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Prognostic factors that influenced survival in 308 Hodgkin's disease pts treated at a single institution between 1972-1989, were analized. Median follow-up was 83 mos (12-210). Pathological staging was performed in 239 pts (78%). Stages I$_A$-II$_A$ recieved *extended field* radiotherapy, stage III$_A$ total nodal irradiation, and the other stages chemotherapy ± boost irradiation.
Overall survival OS and disease free survival (DFS) rates at 15 yrs were 69% and 64% respectively. Poor prognostic factors for OS which were significant in an univariate analysis were age>40 yrs, B-sympthoms, >3 node areas affected, bulky disease, splenic, ESR>60mm/H, hemoglobin<10gr/l, lymphocites account<100mm^3, albumin<35gr/l, stages III$_B$-IV and mixed cellularity and lymphocitic deplection. Regarding the DFS, age, splenic invasion, hemoglobin, lymphocite account and histological types lost signification. In multivariate analysis only stages III$_B$-IV, albumin<35gr/l, age>40 yrs and bulky disease remained independent prognostic discriminants for OS, whereas stages, albumin levels and B-symptoms were significant for DFS.