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IMMUNOHISTOCHEMICAL EVALUATION OF P53-GENE EXPRESSION IN PATIENTS WITH NON-HODGKIN´S LYMPHOMA: CORRELATION TO HISTOLOGICAL SUBTYPE AND EBV-STATUS.

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EBV mechanisms involved in B-cell transformation may include impairment of p53 function. Materials and methods: paraffinembedded material from the diagnostic tumour biopsi of 77 non-immunocompromised NHL-cases (40 of B- and 37 of T-cell-phenotype), diagnosed between 1985 and 1992. All tissue samples had primarily been screened for EBV-encoded small nuclear RNA´s (EBER) using non-isotopic "in situ" hybridasation (39 EBER negative and 38 EBER positive) After this immunohistochemical staining for p53-protein product (DO7-antibody from DAKO, covering wild and mutated p53) was performed. Results: In 4 out of 77 cases (5%) more than 10% of the cells stained strongly positive for p53 (p53 > 10%). In 3 of these p53 was 60% or more. 3 out of 4 p53-positive cases were of T-cell phenotype. 2 of these were also EBER-positive. p53-positive patients had a very poor mean survival (3.5 months, range 0-9 months). In one case, a 31 year old female with anaplastic large cell Ki-1+ T-NHL, localized disease, normal s-LDH-levels, no B-symptoms and good performance status, strong EBER-positivity and strong p53 positivity was found.
This patient died 3 months after diagnosis because of an agressive treatment-refractory disease course. This might suggest that p53- and/or EBV-status could be valuable as additional prognostic factors, or even overrule classical prognostic factors in NHL.

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IMMUNOGENOTYPIC AND IMMUNOPHENOTIPIC STUDIES IN CUTANEOUS T CELL LYMPHOMA. Mateu R, Pujol R.*, Soler J, Hernandez-Bronchud M, Moragas J*. Serveis d'Hematologia i *Dermatologia. Hospital de la Santa Creu i Sant Pau. Barcelona. Spain.

We have analyzed the utility of immunophenotypic and immunogenotypic studies in the evaluation of cutaneous T-cell lymphomas (CTCL). The monoclonal antibodies: CD3, CD4, CD8, CD7 and Leu8; and the gene coding for Cβ T-cell receptor were evaluated in skin biopsies and peripheral blood (PB) of 27 patients with Mycosis fungoide (MF) and in 3 Sézary syndromes (SS) (n=3). Loss of CD7 antigen was found in 10/30 skin biopsies and 3/27 PB whereas loss of Leu-8 was found in 9/30 skin biopsies and 4/27 PB. No correlation between Leu8/CD7 values in skin lesions and PB was detected. Genotypic analysis disclosed monoclonal rearrengement in 5 samples of PB (3/3 with SS and 2/27 MF) and in 12 skin biopsies (4/19 with patch/plaques, 7/7 with nodules and 1/2 with erythroderma). No correlation between the clonality and the loss of CD7 and/or Leu8 antigens was found, thereby raising doubts about the significance of CD7/Leu-8 antigen expression in CTCL.

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TESTICULAR NON-HODGKIN'S LYMPHOMA (NHL)

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In a Danish population-based NHL registry 2687 newly diagnosed patients were registered from 1983-1992. 39 had testicular involvement (TL) (incidence 0.26/10^5/year). Median age was 67 years. Twenty-four cases had localised and 15 disseminated disease. Histologically, all cases were diffuse (65% diffuse centroblastic type). 11% were of T- and 89% of B-immunophenotype. In localised cases where surgery was supplemented by combination chemotherapy (CCT), the relapse rate was 15.4%. The relapse rate for cases with localised disease treated with other regimens was 63.6% ($p < 0.05$). Relapse-free survival was 27.4 and 16.3 months, respectively. Overall 5-year survival was 17%. Adverse prognostic factors at the univariate level were: stage IV, B symptoms, s-LDH elevation and performance score. It is suggested that the treatment of stage I_E/II_E TL should include CCT and CNS prophylaxis.

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Herec-alfa TNF AND INF-alfa COMBINATION THERAPY IN PATIENTS WITH LYMPHOMA MALIGNUM

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Eighteen patients with Lymphoma malignum /stadium IIIB,IV/who developed a resistance on standart chemotherapy were treated with a combination of natural human TUMOR NECROSIS FACTOR and INTERFERON -alfa.Therapy consisted of Interferon-alfa $3x10^6$ IU/m^2 administred sub-cutaneausly on days 1,2 and herec-alfa TNF 150 ug/m^2 daily /30 minute i.v.infusion/for 3 consecutive days /3,4,5 day/.This cycles was repeated every 2 weeks for 5 courses.Side-effects:rigors,nausea,vomiting were observed 93% 89%,68%. Therapeutic findings: complete remission was found in one patient and partial in five subjects.Seven patients had a stable course of this disease.Only in five treated persons in therapeutic effects had not been observed .Patients were followed-up by 6 months .

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IDARUBICIN,CARBOPLATIN,VINORELBINA,PREDNISONE IN RELAPSED AND RESISTENT LYMPHOMAS.M.Musso,E.Iannitto,G.Quintini,F. Porretto,R.Perricone,V.Abbadessa,A.Cajozzo.

We report preliminary results of a pilot study about a polychemotherapeutic association for treatment of patients with relapsed or resistant malignant Linphomas.We till now enlisted 25 patients ,16 males,9 females with age range 18-70 5 patients with H.L. with different Ann Arbor stages and histological types;20 with N.H.L.intermediate and high grade. The schedule of treatment consist of:IDARUBICIN10mg/m^2I.V. (day 1);VINORELBINE 20mg/m^2(day1-5);CARBOPLATIN 300mg/m^2(1° day);PREDNISONE 100mg(day1->5).We planned 6-8 cycles (q21). All patients enlisted were valuable.Approximately 60%(15)of patients respond to this treatment(9R.C.,6R.P.).We noted in approximately 27% (7)of patients a stabilizzation of disease and finally a failure in 12%(3)of patients because a disease progression.One patient died (2° cycle)because gastrointestinal occlusion caused by underlying gastrointestinal disease.We observed low grade of haematological toxicity (WHO 1-2)while extrahematological toxicity was pratically absent, with the exception of a cutaneous erythema-blistered-oedema of limb seat of treatment. CHAIR OF HEMATOLOGY PALERMO ITALY

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A FIVE DRUG REGIMEN FOR INTERMEDIATE AND HIGH GRADE NHL

De Renzo A., D'Arco A., Attingenti E., Pezzullo L., Ferrara F., Pagnini D., Cimino R., Di Girolamo R., Rotoli B. - A multicentric trial coordinated by the Division of Hematology, Federico II University, Medical School, Naples, Italy.

It is still debated which is the most appropriate treatment for eradicating advanced stage intermediate and high grade NHL. Intensive schedules are potentially curative, but harmful and difficult to be administered on out patient basis. In a pilot study we have tried a five drug regimen which is a reinforcement of the classical CHOP: vincristine 2 mg day 1, cyclophosphamide 600 mg/m^2 + idarubicin 10 mg/m^2 day 2, etoposide 100mg/m^2 day 1 to 3, deflazacort 90 mg/m^2 for 5 days. At least six courses with a three week interval were schedule for any type of stage II to IV intermediate and high grade NHL. Up to the time of the abstract, 35 patients entered the study (18 intermediate and 17 high grade, median age 58y, range 34 to 78). Complete remission was obtained in 16/28 evaluable patients; two additional patients who had achieved partial remission after six courses, went into CR after three additional courses. Three patients (all high grade) did not respond and were addressed to a salvage treatment with non cross resistant drugs. No organ toxicity was observed except transient alopecia that occured in all patients. Hematological suppression was moderate, with a nadir on day 14; G-CSF was used in only five patients. Dose reduction and longer interval between courses were needed in four elderly patients (>70 years). Febrile episodes (not requiring hospitalization) occured in 60% of patients; ten patients required RBC transfusion; platelets were never decreased below $50x10^9$/l; hospitalization was never needed. Stage IV patients with liver (one case) and pleural (three cases) involvement went into CR after 1-2 courses; the pleural effusions needed not be drawn in two cases and did not recur after a single drawing in the third. Thus, a five drug regimen including idarubicin and etoposide as main cytotoxic drugs and deflazacort as substitution for prednisone seems effective and well tolerated in intermediate and high grade NHL. A longer follow up and a randomized trial with a conventional four drug regimen are needed to asses a possible superiority of such a protocol.