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THE ROLE OF SURGERY IN THE MANAGEMENT OF THE PRIMARY GASTRIC NON-HODGKIN'S LYMPHOMA

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36 patients with primary gastric non-Hodgkin's lymphoma (PGL) (stage Ie and IIe) were treated at the Centro di Riferimento Oncologico of Aviano (PN) Italy. The median follow up time of the patients was 59 months (range 10 to 117). The preoperative diagnosis of PGL was established by using endoscopy in 70% of the patients. There was understaging in noninvasive methods of diagnosis in compare to laparotomy. The prognostic factors like: stage, grade according to the Working Formulation, size, depth of penetration of the gastric wall and resectability of the tumor, were taken into consideration in the treatment plan which consisted of surgical resection of the gastric lymphoma were feasible and according to the bad prognostic factors escalating adjuvant treatment was included: I group (n=6) patients were treated only by surgery (S), II (n=8) by S + radiotherapy (RT) (n=5) or S + Chemotherapy (CT) (n=3), III (n=17) by S + RT + CT and IV (n=5) by nonresectable S + RT + CT. There were not statistically significant differences in the survival rate, calculated by Kaplan - Meier method, between three first group of patients. Only stage of disease (p=0,048) and resectability of the lesion (p=0,003) had an significant influance for survival. There were no serious complications observed in either S, RT and CT treatment. The estimated survival rate after management was 100%, 75% and 88% respectively for stage Ie (n=21), stage IIe (n=15) and all together. Management of PGL should be optimized according to prognostic factors. We propose the following guidelines for optimizing treatment of patients: I. In stage IE with lesion involving mucosa or submucosa, less then 7 cm, low grade, complete resected can be treated only by S. II. In stage Ie with complete resected lesion, more than 7 cm, tumors not involving serosa, intermediate or high grade can be treated by S and RT or CT. III. In stage Ie complete resected lesion, involving serosa, intermediate or high grade and all in stage IIe with complete resected lesion should be treated by S + RT + CT. IV. With non resectable lesion should be treated by extensive RT and CT. Surgery is indicated for proper staging or for palliative procedure.

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PROGNOSTIC FACTORS IN HODGKIN'S DISEASE (HD), STAGE IIA BULKY TO IV, TREATED WITH COMBINED RADIO-CHEMOTHERAPY.

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From 1/1985 to 8/1993, 133 HD pts (128 newly diagnosed, stage IIA bulky to IV, and 5 in first relapse after RT) were treated with 6 courses of the hybrid MOPP/ABVD regimen followed by RT (STNI + spleen in st. IIA, IIB, III1; TNI + spleen in st. III2, on bulky or residual disease in st. IV), with a total dose of 40 Gy to the bulky or residual disease and 20 Gy to the other sites.
8 pts are not yet evaluable for response; 105/125 (84%) pts obtained a Complete Remission (CR). 5-yr actuarial Overall Survival (OS), Progression Free Survival (PFS), Relapse Free Survival (RFS) are respectively 76%, 71% and 84%.
We evaluated the following prognostic factors for CR, OS, PFS, RFS: gender, age ($\leq$ 40 vs > 40), histology, symptoms (A vs B), sites ($\leq$ 3 vs > 3; $\leq$ 4 vs > 4), stage (II vs III vs IV), bulk > 10 cm (yes vs no; this factor was analysed only in stage III-IV pts, because most of the enrolled stage II pts had bulky disease).
Higher probability of CR was associated with gender (male, p = 0.036), $\leq$ 4 sites (p = 0.017), no B symptoms (p = 0.002), no bulky disease for stages III-IV (p = 0.001). Favourable prognostic factors for 5-yr OS are: $\leq$ 4 sites (p = 0.042), no bulky disease for stages III-IV (p = 0.020), lower stage (p = 0.034); for 5-yr PFS: $\leq$ 4 sites (p = 0.0001), no B symptoms (p = 0.003), no bulky disease for stages III-IV (p = 0.002); for 5-yr RFS: $\leq$ 4 sites (p = 0.003).
Conclusions: $\leq$ 4 sites of disease and absence of bulky lesions are the strongest predicting factors fors a better outcome in pts with advanced Hodgkin's disease.

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DETECTION OF CLONAL T CELL POPULATION IN PERIPHERAL BLOOD OF PATIENTS WITH CUTANEOUS MALIGNANT T-CELL LYMPHOMA

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The use of the Polymerase Chain Reaction (PCR) to detect monoclonality in lymphatic skin infiltrates is used in the routine diagnosis of cutaneous malignant lymphomas in our department. We now asked wether this extremely sensitive method would allow the detection of the malignant clone in peripheral blood, since cutaneous T-cell lynphomas (CTCL) derive from recirculating skin-homing T-cells. From 19 patients with pleomorphic T-cell-lymphoma (n=7) or mycosis fungoides (mf, patch stage n = 10, tumor stage n =2) 10 ml of heparinized blood was drawn. Mononuclear cells were isolated (Ficoll gradient) , the DNA was extracted (in average out of 12x 10^6 cells) and a PCR with 12 specific primers for the V-and J-regions on the TCR gamma chain gene was performed . PCR-amplification products were separated by Temperature-Gradient-Gel-Electrophoresis (TGGE).
All patients (7) with pleomorphic T-cell-lymphoma showed initially a clonal gene-rearrangement in the skin biopsy as well as in the peripheral blood. 2/2 patients in tumor stage of Mycosis fungoides showed a persisting monoclonal T-cell population in skin and blood with a progressive clinical development. In only 2/10 cases of patch stage mf, initially a clonal gen-rearrangement was detected in blood and skin. These data show for the first time, that in pleomorphic T-cell lymphomas as well as in all cases of advanced stages and some patients with early stages of mycosis fungoides, clonal T-cells are present in the peripheral blood in an amount detectable with PCR. This new understanding of CTCLs as deseases involving the complete circulation system (i.e. skin, lymph nodes (?), blood) will directly influence future therapeutic strategies.

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407 patients (pts) with AIDS-related non-Hodgkin's lymphoma (AIDS-NHL): the experience of the GICAT (Italian Cooperative Group on AIDS and Tumors) with emphasis on the prospective treatment of 93 pts at a single institution.

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Since november 1986, we have collected data on 407 pts with peripheral AIDS-NHL observed in several Italian institutions of the GICAT. 62% of pts were intravenous drug users (IVDUs) in accordance to the overall epidemiology of HIV infection in Italy, 83% were males, the median age was 30 years. At diagnosis of AIDS-NHL, CD4 < 100/mm^3 were detected in 46% of the pts, and opportunistic infections (OIs, C1 according to CDC) preceded or accompanied the NHL in 41% of the pts. Immunoblastic and Burkitt were diagnosed in 58% and 20% of the pts, respectively; advanced (III and IV) stage and B symptoms were present in 80% and 69% of the pts, respectively. Median survival of the overall population was 6 months; by the Cox model four factors were associated with a significantly shorter survival: advanced stage, heterosexuality, no treatment received and not having obtained a CR. At the Aviano Cancer Center, in the same period of time 93 of these pts have been treated according to prospective protocols. Based on HIV-related prognostic factors pts with unfavourable histology and stage III and IV were treated with intensive third generation chemotherapy regimens (group 1, usually with CD4 > 200, good PS and without OI), with palliative chemotherapy with just 1 or 2 drugs or local RT (group 3, usually with CD4 < 100, poor PS and with OI) or with standard CHOP-like chemotherapy regimens (group 2, the remaining pts). The table reports the parameters that reached statistical significance in the comparison between the 3 groups of evaluable pts.
A significantly higher CR rate (61%) has been observed in group 1 pts, but with a concomitant increase of OIs during CT and follow up (66%), in comparison to group 2 pts (48% and 38% respectively). However group 1 pts had a 1.5 decreased risk of dying in comparison to group 2 and 3 pts. Overall, 13 pts with a CR lasting for at least 2 years had a 42-month median survival with none of such pts relapsing even after 6 years. In conclusion, we have observed a large number of peripheral AIDS-NHL, mainly with immunoblastic and Burkitt subtypes, advanced stage and B symptoms. In the prospective treatment at a single institution, intensive chemotherapy regimens were associated both to higher CR rate and higher OIs during CT and follow up, with some pts experiencing long survival and possibly cure. The potential role of bone marrow growth factors in order to decrease bone marrow toxicity and more efficacious OI prophylactic therapy are currently prospectively tested. Supported by AIRC grants.

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THE CLINICAL SIGNIFICANCE OF MOLECULAR MONITORING IN THE MANAGEMENT OF PATIENTS WITH FOLLICULAR LYMPHOMAS.

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Background: **The t(14;18) chromosomal translocation, which results in the bcl-2/JH gene rearrangement, is a consistent molecular feature of follicular lymphomas (FL) that can be detected in the large majority of patients by DNA analysis using the polymerase chain reaction (PCR).**
However, the utility of molecular monitoring in the clinical management of the patients with FL is still controversial.
Aim and methods: **Since 1989, we began a prospective study to assess the utility of bcl-2/JH PCR analysis of peripheral blood (PB) and bone marrow (BM) in FL patients. Samples have been analysed prior and post treatment and during the follow up.**
Results: **bcl-2/JH gene rearrangements were detected in BM and PB at diagnosis in approx. 60% of FL patients with histologically negative BM . We found a very close correlation beetween the bcl-2/JH positivity in the PB and the corresponding BM sample at diagnosis: paired samples showed concordance in approx. 95% (74/77) of patients. This striking correlation may no longer be true after treatment. In 4 cases the PB has become negative, while the PB remained clearly positive after non-aggressive chemotherapy (single-agent chlorambucil). However, the clinical significance of this finding is unclear: we could also demonstrate the persistence of bcl-2/JH positive circulating cells in some long remission FL patients.**
The possibility of eraticating the tumor with very aggressive treatment is another controversial issue. We used the PCR assay for evaluating the efficacy of a sequential myeloablative chemotherapy program followed by autotransplantation with reinfusion of peripheral stem cells. Preliminary data (5 analysed cases) seems to suggest that patients achieving a molecular remission (i.e. bcl-2/JH positive cells no longer detectable in their PB by the PCR assay) can have a better outcome, while the persistence of bcl-2/JH positive cells might be predictive of early relapse.