

30.5–47%) was the lower than that of large cell, T-cell lesions (54.9, range 5–80.5%) whilst Burkitt's lymphoma lesions had the highest mean apoptotic fractions (68.5, range 48.5–87%).

Conclusions: Apoptotic fraction of MNHL in childhood affects mean nuclear volume and may explain difficulties in classifying lesions on nuclear size and appearance only. However, the relationship between the mean, although somewhat variable, apoptotic fractions of Burkitt's lymphoma versus large cell lesions and present treatment outcome (75–85 versus 50–70% survival) justifies further study.

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PUBLICATION

Bendamustin – Relapse therapy in patients with low grade non Hodgkin's lymphoma (NHL)

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Purpose: Low grade NHL rarely are showing complete and sustained remissions after first line cytostatic therapy making new options for relapse therapy necessary.

Methods: Since January 1995, 27 patients (pts) with advanced and refractory low grade NHL (lymphocytic 13, cbcc 10, immunocytic 2, centrocytic 2) were included in this monoinstitutional trial. Pts were pretreated with 1–4 (median 2) cytostatic combinations. Bendamustin was given dependant on weight (<50 kg: 100 mg, >50 kg: 200 mg) as an one-hour infusion on two consecutive days every three weeks until stable disease (NC), partial (PR) or complete remission (CR) could be documented. In case of further progression, treatment was stopped.

Results: So far, 23 pts are evaluable for response and toxicity. 2 pts (9%) achieved CR, 14 pts (61%) PR and 3 pts (13%) NC, while 4 pts (17%) showed PD. The preliminary median remission duration is 8 months (range, 2–14). Side effects were mild and restricted to nausea and myelosuppression WHO-grade 1 and 2.

Conclusions: Bendamustin is an active and well-tolerated cytostatic drug in relapsed low grade NHL. Further controlled investigations are warranted.

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PUBLICATION

Magnetic resonance imaging of bone marrow versus biopsy in malignant lymphoma

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Purpose: Bone marrow biopsy of the posterior iliac crest is routinely performed for staging of malignant lymphoma. Abnormal magnetic resonance imaging (MRI) signals of bone marrow is also reported to be indicative of bone marrow involvement. In this study, we aimed to evaluate the role of MRI in detecting bone marrow infiltration in patients with malignant lymphoma.

Methods: 60 patients with malignant lymphoma were studied. Patients were evaluated prior to initiation of the treatment. Unilateral bone marrow biopsy of the posterior iliac crest and MRI of lumbar spine were performed. Analysis of the results were based on the assumption that histologic examination of core biopsies of the posterior iliac crest is the ultimate method of detecting bone marrow involvement.

Results: Among 60 patients evaluated, MRI findings of 52 patients were deemed to be positive or negative for radiologic evidence of unequivocal tumor involvement by 3 radiologists. MRI intensity were suspicious in 8 patients. The sensitivity and specificity of MRI of 52 patients were found to be 86% and 90% respectively.

Conclusion: Although limited in number, these results suggest that MRI of bone marrow is a fairly sensitive, noninvasive method and might be of potential value in detecting bone marrow infiltration in malignant lymphoid neoplasms and can be utilised, as a useful adjunct to standard staging procedures.

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PUBLICATION

Initial clinical features in patients of various age with non-Hodgkin's lymphomas

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Purpose: The initial clinical features of non-Hodgkin's lymphomas (NHL) were studied in 606 patients of various age.

Results: Only high-grade NHL were diagnosed in childhood. Lymphomas of high-grade malignancy were predominating in adults too, but the frequency of low-grade NHL was increasing with the age. Fifty-five per cent of cases NHL in children originated in extranodal tissue. Primary NHL of various lymph nodes were present in most adult patients. Favoured extranodal sites in adults and children included the digestive tract and Waldeyer's ring. The most frequent sites of primary NHL of digestive tract were the stomach in adult and the intestines in children. Primary NHL of the spleen were more frequent in adults, especially over 60 years. Retroperitoneal and mesenteric lymph nodes were most often involved in children, mediastinal lymph nodes in teen-agers, peripheral lymph nodes – in adults.

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PUBLICATION

Combined chemotherapy-radiotherapy in I-II stage of non-Hodgkin's lymphomas

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Purpose: We have reported the results of combined chemotherapy-radiotherapy in 98 previously adult patients with localized non-Hodgkin's lymphomas (NHL; stage I-II-48, stage II-II-50). There were 78 patients with high- and intermediate-grade and 20 patients with low-grade NHL.

Methods: All patients received 3 courses of CHOP in I phase, involved radiotherapy in II phase, and final 3 courses of CHOP chemotherapy in III phase with following maintenance therapy.

Results: Thirty seven (92.5%) patients had a complete response and 2 (5.0%) had a partial response in I-II stage of high- and intermediate-grade NHL. Twenty two (57.3%) patients from unfavorable group had a complete response and seven (18.4%) had a partial response in II-II stage. The complete remission rate was achieved in all patients with low-grade NHL in I-II stage and in 11 (91.7%) cases with II-II stage. The actuarial survival at five years in unfavorable group was 79.4% in I-II stage and 40.0% – in II-II stage. The actuarial survival at five years for favorable group was 100% in I-II stage and 73.3% – in II-II stage.

1223

PUBLICATION

Relationship between rate of "in-field" bone marrow regeneration and radiation dose in patients with Hodgkin's disease

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Purpose: To evaluate relationship between absorbed dose and rate of irradiated BM regeneration after combined modality treatment (CMT) of patients with Hodgkin's disease (HD).

Materials: BM scanning was performed 1–84 months after CMT of 69 patients with HD. Absorbed doses ranged from 28–32 Gy to 38–45 Gy. BM activity was estimated semiquantitatively: grades 1–2 – no or some activity, grades 3–4 – partial or complete regeneration.

Results: Irrespective of absorbed dose (in the range of 28–45 Gy) during 1–5, 9 months after CMT hematopoietic activity was reduced in 70 of 71 irradiated regions. 6–12 months after radiotherapy scintigraphic signs of BM regeneration (grades 3–4 of tracer uptake) were mentioned in 12 of 17 areas (71%) irradiated with 28–32 Gy and in only 5 of 16 (28%) – with 38–45 Gy ($p < 0.05$). Thirteen and more months after the end of CMT percent of BM regeneration was still dose dependant: 77% (in 44 of 57 areas) – after 28–32 Gy and 51% (in 36 of 71 areas) after 38–45 Gy ($p < 0.05$).

Conclusion: After irradiation with 28–32 Gy rate of in-field BM regeneration is higher than after irradiation with 38–45 Gy. BM recovery after conventional CMT of patients with HD is dose dependant.

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PUBLICATION

Results of mantle irradiation alone in adult patients with clinical stage (CS) I and II Hodgkin's disease (HD) with low probability of abdominal involvement and good prognostic factors

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Background: Since 1988 we have used mantle irradiation alone for patients with CS I or II HD with low probability of abdominal involvement at laparotomy

(i.e.: patients with NS or LP histology, no B symptoms, and a No. of involved sites ≤ 4 ; *Cancer* 1989, 63: 1799–803) and no more than one of the negative prognostic factors (male sex, age > 40 , ESR > 40 , No. of involved sites > 2 , or bulky palpable nodes) identified in another analysis.

Patients and Methods: Between July 1988 and December 1994 we treated 27 previously untreated adult patients with CS I or II HD without bulky mediastinal disease who had a predicted probability of abdominal involvement $\leq 10\%$ and no more than one negative prognostic factor. Twenty-six patients received RT to mantle field only and were considered evaluable and one patient that received subtotal nodal RT was excluded. Eight patients had CS I and 18 had CS II HD, 21 patients had NS and 5 had LP histology. Negative prognostic factors were male sex in 10 patients, ESR > 40 in two, and No. of sites involved > 2 in 4 patients. **Results:** With a median follow-up of 62 months, 20 patients remain with no evidence of relapse and 6 have relapsed. The 5-year DFS was 76% and the 5-y survival was 100%. The 5-y DFS was 88% in patients with CS I and 71% in patients with CS II. In patients with CS II disease, the risk of relapse increased as the predicted probability of abdominal involvement increased ($p = 0.06$; Logrank test for trend).

Conclusions: The group of patients with CS I HD defined above can be spared the morbidity of laparotomy and subdiaphragmatic RT and still have high probability of DFS. Further study is necessary to establish what subgroup of CS II patients would be suitable for this approach but our data suggest that the predicted probability of abdominal involvement could be useful to identify that subgroup.

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PUBLICATION

Relation between IL-10 and IL-12 secretion in Hodgkin's disease (HD)

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Advances in tumor immunobiology have contributed to explain the mechanisms of the cancer-related immunosuppression. IL-10, mainly produced by Th2-lymphocytes, inhibits in vitro the secretion of the two main antitumor cytokines IL-2 and IL-12. IL-2 serum levels proved to be low in several advanced tumors, including HD. In contrast data from our own study, suggest increased IL-12 serum levels in untreated HD pts. Since in vitro studies showed that IL-12 may inhibit the secretion of the suppressive cytokine IL-10, this study evaluated the relation between IL-12 and IL-10 secretion. IL-10 serum levels of 68 untreated pts were correlated to those of IL-12. Characteristics were: M/F: 41/27, median age 27, range 16–61, A/B symptoms: 36/32, stage I + II/III + IV: 49/19, ≤ 3 / > 3 sites: 36/32. IL-10 and IL-12 serum levels were measured by enzyme-linked immunoassay kits, and normal values (95% confidence limits) ranged from 0 to 6 pg/ml and 10 to 89 pg/ml respectively.

High levels of IL-10 were observed in 31/68 pts (46%), and abnormally high serum levels of IL-12 were discovered in 27/68pts (40%). There was no correlation between IL-10 and variables analyzed as stage, disease extent and B symptoms. No significant difference in IL-10 mean serum levels was observed between pts with high IL-12 compared to those with low or normal IL-12 values (18 ± 11 vs 8 ± 1 pg/ml; median \pm S.E.).

These preliminary data demonstrate an enhanced IL-10 secretion in HD. Moreover, despite the in vitro inhibition of IL-12 on IL-10 secretion, we found no correlation between IL-12 and IL-10 production in HD pts.

1226

PUBLICATION

Combined modality treatment and adjuvant lumbo-splenic radiotherapy (RT) in supra-diaphragmatic (SD) clinical stage (CS) I–II Hodgkin disease (HD) results in decreased rates of infra-diaphragmatic (ID) nodal relapses (R)

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From 10/81 to 9/88, 262 patients (pts) aged 15 to 65 yr with CS I–II HD were enrolled in the POF 81/12 trial. 3 courses of ABVD (Adria 25, Bleo 10, Velban 6, DTIC 375 and MPred 120 mg/m² on d1&15). Pts in complete or partial remission (CR or PR) received extended field (F) RT (involved F 40 Gy, adjacent F 30 Gy, lumbosplenic 30 Gy). CR was obtained in 258 pts. In 12/96, 23 R (8.9%) were observed 3 to 130 mo (median 32) after the end of RT. 3 pts (1.2%) had extranodal (EN) R, 15 pts (5.8%) had nodal (N) R, 5 pts (1.9%) had simultaneously EN and N R. Only 5 pts (1.9%) had ID nodal R. (1 in lumbosplenic region, 1 in pelvis and the 3 others in ID + SD \pm EN areas. Among 15 pts who had a 2nd CR (65.2%), 6 had a 2nd R out of which 1 was ID. Thanks to primary CT plus prophylactic lumbosplenic RT, a very low rate of ID R (1.9%) was obtained in clinically staged SD HD. No life-threatening infection was observed during initial treatment and only 1 pt acquired hypertension ($\geq 150/100$ mm Hg).

Endocrine tumours

1227

ORAL

Differences in photosensitizer induced fluorescence of rat adrenal chromaffin cells and pheochromocytoma cells (PC 12)

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Adrenal glands photosensitized with meso-tetra (hydroxyperoxy)chlorin (mTHPC) exhibit an intense fluorescence. The objective of our experimental study was to investigate whether adrenal medullary cells and pheochromocytoma cells of the rat (PC 12) show a selective uptake of mTHPC. The overall objective was to evaluate whether photodynamic therapy may be feasible for adrenal tumours.

4 Wistar rats were injected mTHPC (0.5 mg kg⁻¹) 48 hours before perfusion, which was carried out after a lethal dose of Nembutal® with Zamboni fixative. 4 Wistar rats received reserpine (2.5 mg/kg BW sc; 5 days q.d.) and treated in the same way as the first group. Shock frozen adrenals were cut into 20 μ m sections. PC 12 cells were incubated with mTHPC (0.5 mg/l culture medium) for 24 and 48 hours. Examination of tissues and cells was performed by fluorescence microscopy.

Adrenal medullae did not show any fluorescence except for singly scattered cells. However reserpine treatment, which induces pheochromocytoma in rats, enhanced medullary fluorescence, with several cell clusters of intensely fluorescing cells. The adrenal cortical cells showed an intense cytoplasmatic fluorescence, not being altered by reserpine. In vitro, viable PC 12 cells showed an intense cytoplasmatic mTHPC-induced fluorescence. Cells lying singly or in small groups showed a more intense fluorescence than confluent cells.

The present results implicate for the first time the possibility of laserlight-induced fluorescence diagnosis and photodynamic therapy of adrenal tumours.