1188 POSTER*

Differences in cell proliferation fraction masked by apoptotic fraction in childhood lymphoma (MNHL)

Lynne M. Ball, C.L. Lannon, S. Murray, J. Tam, M. Henry, C. Isenor, A. MacKay, K. Laybolt, D. van Velzen. *Departments of Haemato-Oncology, Pathology IWK/Grace Health Centre, Halifax N.S., Canada*

Purpose: In-situ labelling for apoptosis derived DNA fragments shows previously unappreciated, high and highly variable apoptosis fractions which may influence calculated proliferation fraction and obscure relevancy to treatment response. We studied a defined series of childhood lymphoma to assess the relevance of apoptosis.

Methods: Consecutive unselected, primary diagnostic samples of 12 Burkitt's lymphoma (M: 6, F: 6, mean age: 8 y 3 m, range: 4 y 2 m–14 y) and 16 diffuse large cell lymphoma (9 T-cell, 7 B-cell, M: 11, F: 5, mean age: 9 y 9 m, range: 1 y 5 m–16 y 8 m) were studied by Frag-EL (CalBiochem, USA) and S-phase immunoperoxidase labelling using cDNA defined Moab for the Ki-67 antigen (MM1, NovoCastra, UK). Quantitation using established image analysis (Quantimet 570C).

Results: The results are summarised as follows:

Group	Frag-EL%	Ki-67%	Apopt. corr. prol. fr
Burkitt's	68 5# (48.5–87)	25.2 (14–54 5)	75 (38–100)*
diffuse,	48.5 (5–80.5)	34 (7–66)	69 (12–100)
T-cell	54.9 (5–80.5)	34 8 (15–66)	80 (27–100)**
B-cell	40.2 (30 5–56.5)	32.9 (7–50)	56# (12–100)***

[*: Burkitt's: 4/12 100%; **: T-cell: 4/9 100%; ***: B-cell: 1/7 100%] [#: probability of non-difference <0.05]

Conclusion: Childhood lymphoma exhibits highly variable (high) fractions of cells committed to apoptosis, especially Burkitt's lymphoma. Recalculation of fraction of proliferating cells of non-apoptotic cells only shows B-cell diffuse large lesions to have lower proliferation fraction than both Burkitt and diffuse T-cell lymphoma. The relationship, previously not recognised, requires re-assessment.

1189 POSTER*

Evaluation of residual or recurrent malignant lymphoma by FDG-PET

M. Sökler[1], B.M. Dohmen[2], C. Bokemeyer[1], W. Brugger[1], A. Kopp[3], R. Bares[2], L. Kanz[1]. *[1]Department of Internal Medicine II; [2]Department of Nuclear Medicine; [3]Department of Radiology, Eberhard-Karls-University, Tübingen, Germany*

Purpose: The differentiation between residual/recurrent vital tumor and scar or inflammatory tissue is a common problem in the treatment of patients with malignant lymphoma. Morphological criteria like tumor size or shape investigated by CT or MRI are insufficient to detect vital lymphoma tissue. Therefore, the current study evaluates FDG-PET for the detection of viable lymphoma tissue in morphologically suspicious lymphatic nodes.

Methods: 33 patients with residual lymphoma (n = 16) or suspected tumor recurrence (n = 17) of either Hodgkin's-disease (n = 15) or high-grade-NHL (n = 18) were enrolled in the study. Static, attenuation corrected PET scans of the known lymphoma sites were obtained after i.v. injection of 350 MBq 18-FDG. Image analysis was visual and used increased focal FDG-Uptake as a sign of malignancy. Patients were either clinically followed (n = 17) or histology of the suspected lymphatic node was obtained (n = 16).

Results: In 13 out of 16 residual lymphoma masses correct tissue classification could be achieved by FDG-PET (6 true positive (TP), 7 true negative (TN)). One false positive result was obtained 8 weeks after radiotherapy. In 2 cases tumor recurrence occurred 2 resp. 5 months after negative PET. In patients with suspected tumor recurrence FDG-PET was correct in 15 of 17 patients (14 TP, 1 TN). False positive results were obtained in a case of a histologically proven lymphatic hyperplasia and in a case of sarcoidosis 3 months after high-dose-chemotherapy for high-grade-NHL. Thus, FDG-PET showed a 91% sensitivity and 73% specificity. Positive and negative predictive value were 87% and 80%.

Conclusion: FDG-PET appears to be a sensitive technique for the diagnosis of residual as well as recurrent malignant lymphoma. Inflammatory disease may cause false positive results. Small tumor cell clusters in residual tumors leading to relapse after a longer disease-free interval might be missed.

1190 POSTER*

Favourable prognosis after late relapse in Hodgkin's disease

R. García-Carbonero, A. Arcediano, L. Paz-Ares, J. Lahuerta, R. Colomer, H. Cortés-Funes. *Division of Medical Oncology, Hospital Universitario Doce de Octubre, Madrid, Spain*

Background: Most of the relapses in Hodgkin's disease (HD) occur in the first two years following diagnosis, but some appear with longer observation time. The aims of this study were to define incidence, clinical course and prognostic factors for late relapse (LR) in Hodgkin's disease. For this purpose we defined LR as recurrence that occurs in patients who achieved a complete remission that lasted at least 24 months.

Patients and Methods: From 1974 to 1994, 375 patients with newly diagnosed HD were treated at our institution. Of these, 223 patients remained free of disease for at least two years. In addition, other 26 patients had been in complete remission for a minimum of 24 months after salvage treatment. Thus, 249 patients were identified to be at risk of LR, and they were the study subjects. The median age was 29 years. The clinical (c) or pathological (p) stage was pI in 19 patients, cI in 24, pII in 58, cII in 48, pIII in 30, cIII in 34, pIV in 14 and cIV in 24. Ninety patients presented B symptoms at diagnosis and 87 had bulky disease. Treatment consisted of radiotherapy in 68 patients, chemotherapy in 68 and both in 113.

Results: With a median follow-up of 125 months (range: 22–287 months), we observed 29 LR (11.6% of the patients). The estimated relapse rate at 15 years was 17.7%. Recurrence occurred after a median disease free interval of 55 months (range: 25–152 months), and involved sites of previous disease in 70% of the patients. Fifty-four per cent of the patients were asymptomatic at relapse and physical examination was the most effective diagnostic procedure. Univariate analysis of prognostic factors showed that patients with extranodal disease, age over 30 years, and ECOG $\geq$ 2 were at greater risk for late relapse ($p < 0.05$). At a median of 44 months (range: 6–127 months) following therapy for LR, 19 patients continue alive and free of disease, two patients are alive with HD and 8 have died (one without HD). The expected survival after LR was 68% at 5 years. When we compared overall survival (OS) of patients with late relapse with OS of non relapsing patients, the observed differences were of borderline statistical significance ($p = 0.051$).

Conclusion: The actual incidence of LR emphasizes the need for continuous follow-up of patients treated for HD. Late relapses, if properly managed with standard therapy, have a favourable prognosis.

1191 POSTER*

Skin changes in successfully treated Hodgkin's disease patients

E. Stockfleth, H.T. Flammann[2], T. Meyer[2], H. Pfister[3], D.K. Hossfeld[1], E. Christophers. *Department of Dermatology, University Hospital of Kiel; [1]University Hospital of Hamburg-Eppendorf; [3]University of Cologne; [2]IPM Hamburg, Germany*

Purpose: Cured Hodgkin's disease (HD) patients face an increased risk of secondary malignancies and skin alterations. Our main interest was to look for specific (I), unspecific (II), infective (IIIa), noninfective (IIIb) and skin cancer (IV) changes.

Methods: We made a complete examination of the skin in 50 HD patients and analyzed skin tumors and the serum of the patients for oncogenic Human Papillomavirus (HPV) types, using general -PCR, Western Blot and ELISA

Results: Cutaneous lesions were detected in nearly all patients. We found (I) 66% dysplastic naevi, (II) 52% hyperpigmentation-, 44% dry skin, 16% unclear pruritus; (IIIa) 18% herpes zoster, 44% herpes labialis, 8% genital herpes, 36% palmar warts, 28% plantar warts, 12% genital warts, 4% Epidermodysplasia verruciformis (EV) lesions, (IIIb) 36% fungal infections, (IV) 10% basal cell carcinoma and 4% Erythroplasia of Queyrat. Almost all premalignant and malignant lesions were located on skin areas that had been treated with radiotherapy. Oncogenic HPV DNA were detected in nearly all skin tumors. We found antibodies against oncogenic HPV-types such as HPV8 (48% positive) and HPV16 (40% positive)

Conclusion: Since cured HD patients face an increased risk of skin alterations, the clinical demonstration, especially of precancer and cancer skin lesions and the demonstration of potentially oncogenic HPV-types, underline the importance of careful follow-up to facilitate early prognosis and treatment of such lesions.