year before developing breast lymphoma. 19 pts were eligible (1 male and 18 female) Median age was 54 (Age>60 was 31.6%), with 68.4% of patients presented with breast mass with Median tumor size 5cm (range 3−6 cm). 31.6% presented with diffuse breast mass with clinical picture of inflammatory disease, they were clinically thought to have a primary breast carcinoma. The diagnosis of lymphoma was made by excisional, inscional, and repeated FNAB biopsy in 52.6%, 10.5%, and 36.8% respectively. Diffuse large B cell lymphoma (DLBCL) was the most common histological subtype seen in 13 pts (68.4%) patients. 5 pts had MALT lymphoma and Mantle cell type was seen in 1 pt (26.3% and 5.3% respectively). Left side involvement was 57.9%. Axillarly LN was detected in 47.4%. LDH was elevated in 68.4%. Stage IE/IIE was 78.9%. 2 pts had BM involvement (10.5%). Mastectomy was done in 26.3% and 60% of them relapsed. 17 pts received chemotherapy (Median 6 cycles (range 0−8) and 15 pts received combined chemo and radiotherapy. Median radiotherapy dose 30 Gy (range 20−40 Gy). Overall response (ORR) was 84.2%, CR/CRU 68.4% with a median follow up 2.4 years (range 0.3−9.7). 9 pts (36.8%) relapsed locally and systemically. 2 pts (10.5%) had a CNS relapse 2 leptomeningeal involvement. The median time to CNS relapse was 13.2mos (8.4−18 mos). In univariate analysis (LDH ($p = 0.02$), IPI ($p = 0.09$), type of relapse ($p = 0.01$) and pathology type ($p = 0.8$). Actuarial 5y Overall Survival (OS) was 56.3% and progression free Survival (PFS) was 51.4%.

Conclusion: PBL can be successfully treated by limited surgery, chemotherapy and radiotherapy. CNS relapse was observed in our series of patients. Rituxmab and CNS prophylaxis should be considered in prospective clinical trial.

Keywords: Primary breast lymphoma, presentation, and treatment outcome.

9220 POSTER

Burkitt's lymphoma-derived cells are sensitive targets for the oncolytic activity of rat parvovirus H-1PV

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Background: Oncolytic viruses are recently emerging as promising candidates for the treatment of human cancers. The rat parvovirus H-1PV has been shown to selectively kill human cancer-derived cell lines *in vitro* and to suppress rat and human tumors in animal models. Previous studies have shown that some transformed B cells are H-1PV targets *in vitro*. The present study aims at investigating, both *in vitro* and *in vivo*, H-1PV potential as a therapeutic agent against human lymphoma.

Materials and Methods: A panel of Burkitt's lymphoma (BL)-derived cell lines was used to study H-1PV-induced oncolysis *in vitro*. Infectious parvovirus progeny production was measured by a modified plaque assay. Immunofluorescent staining of lytic Epstein-Barr virus (EBV) proteins was used to detect EBV latency break. Propidium iodide/Annexin-V staining of H-1PV-infected cells was performed to reveal the type of death. For the *in vivo* studies, BL cells were engrafted in SCID mice. Tumor-bearing animals received a single intratumoral H-1PV dose at either early or late time-points after tumor initiation. RT-PCR and Southern blotting were used to detect H-1PV expression and replication in treated tumors.

Results: BL-derived cells were found to be highly sensitive H-1PV targets *in vitro*, irrespective of EBV persistence or rituximab resistance. Parvovirus-infected cells died through necrosis, and death was not due to lytic EBV replication since no signs of EBV latency break could be observed. BL cells supported a productive H-1PV infection. In contrast, normal healthy donor B lymphocytes were not permissive for H-1PV infection. *In vivo*, complete tumor regression accompanied with long-term survival was observed, even when the parvovirus was applied at advanced stages of lymphoma development. H-1PV DNA replication and extensive necrosis, correlating with accumulation of viral cytotoxic NS1 proteins, were observed in regressing tumors.

Conclusions: Altogether, *in vitro* and *in vivo* data suggest that H-1PV deserves to be further considered as a candidate for the treatment of human non-Hodgkin B-cell lymphoma.

9221 POSTER

A subset of chemotherapy-refractory diffuse large B-cell lymphomas is characterized by constitutive upstream activation of the intrinsic apoptosis pathway

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Background: Inhibition of the apoptosis cascade is an important cause of therapy resistance in diffuse large B-cell lymphomas (DLBCL). In this study, we investigated the functionality of the intrinsic apoptosis pathway in lymphoma cells of thirty DLBCL biopsies.

Materials and Methods: DLBCL patient samples were investigated for their expression levels of apoptosis-related genes using reverse transcription-multiplex ligation-dependent probe amplification (RT-MLPA) analysis. Functional analysis of the intrinsic, caspase-9-mediated pathway was done using fluorescence-activated cell sorting analysis, Western blot analysis, and immunohistochemistry.

Results: Two DLBCL groups were identified using RT-MLPA analysis; one group with low expression levels of both pro- and anti-apoptotic genes and one group (54% of the DLBCL) with high expression levels of these genes. DLBCL with high expression levels of pro- and anti-apoptotic genes frequently appeared to be refractory to clinical chemotherapy. Functional analysis in these latter DLBCL samples and DLBCL cell lines with comparable expression profiles revealed high levels of spontaneous caspase 9 activity, mitochondrial membrane depolarization and release of cytochrome c in the cytosol, without induction of apoptosis, indicating disruption of the apoptosis pathway downstream of caspase 9 activation. Furthermore, high levels of p53 were found in most of these DLBCL patient samples and DLBCL cell lines. Upstream inhibition of the intrinsic pathway with a p53-inhibitor resulted in a decrease in caspase 9 activity in DLBCL cell lines.

Conclusions: We conclude that the intrinsic caspase 9-mediated apoptosis pathway may be constitutively activated with concomitant downstream inhibition of the convergence apoptosis pathway in chemotherapy-refractory DLBCL. Constitutive caspase 9 activation might be caused by stabilization of p53 expression.

9222 POSTER

Association of polymorphisms in cytokine genes with Diffuse Large B Cell Lymphoma and its outcomes in Omani Arabs

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Background: The study was carried out to see whether polymorphisms in cytokine genes were associated with Diffuse Large B cell Lymphoma (DLBCL) in Omani Arab patients. Additionally, we studied whether these polymorphisms correlated with either the prognostic features at presentation, or with overall survival.

Patients and Methods: Over the study period of 5 years, a total of 84 patients with DLBCL were evaluable, the DNA was examined for mutations in IL-10 (T-3575A) and TNF-α (G-308A) genes using PCR, and restriction fragment length polymorphism (RFLP). DNA was also extracted from 115 age and gender matched controls. Clinical data were extracted from the clinical database, and the associations were studied using chi-square test. Correlation with survival was studied using the method of Kaplan and Meier. The study was approved by the Medical research and Ethics Committee.

Results: Median age was 47 years, and there were 46 males and 34 females. Homozygous form of IL-10 (T-3575A) was associated with DLBCL (OR 3.181; 95% CI 1.020−9.926; $p = 0.046$), whereas, no association was found with TNF-α (G-308A) polymorphism. TNF-α (G-308A) was strongly associated with advanced stage of the disease ($p = 0.009$). Also the combination of mutant form of IL-10 and TNF-α was associated with an advanced stage of the disease ($p = 0.026$). Heterozygous form of IL-10 (T-3575A) was associated with a poor overall survival (median survival 22 months versus 60 months), whereas, polymorphic TNF-α (G-308A) gene did not affect the overall survival.

Conclusion: Homozygous form of mutant IL-10 gene may be implicated in the genesis of DLBCL in Omani patients. Mutation in TNF-α gene was associated with advanced stage, whereas, mutation in IL-10 gene was associated with inferior survival.