

P60. HYPOXIA-REGULATED PROTEINS IN GASTRIC CANCER: CORRELATION WITH DISSEMINATED TUMOR CELLS AND CLINICAL OUTCOME

S. Osinsky^a, D. Gluzman^a, G. Olijnichenko^c, L. Bubnovskaya^a, I. Ganusevich^a, D. Osinsky^b, S. Merentsev^a, L. Gumenjuk^a. ^aInst. Exp. Pathol. Oncol. Radiobiol., NASU, Ukraine; ^bInst. Oncology, AMSU, Ukraine; ^cMunicipal Oncological Hospital, Kiev, Ukraine.

Background: It is known that tissue hypoxia has a positive impact on malignant progression. Our study was aimed to examine the correlation between hypoxia-regulated proteins (HRP), disseminated tumor cells (DTC) and clinical outcome in gastric cancer (GC).

Methods: One hundred and thirty three naïve patients with primary GC who underwent surgery were included in the study. All patients have been informed about investigation. Hypoxia within tissue was evaluated using ³¹P NMR spectroscopy (PME/Pi), expression of hypoxia-inducible factor-1 α (HIF-1 α) and CD34 (microvessel density – MVD) in tissue were assessed using immunohistochemistry, gelatinases (MMP-2 and -9) activity was determined with zymography. DTC in bone marrow (BM) were detected using immunocytochemistry. Statistical analyses were done using NCSS/PASS package (NCSS, UO, USA).

Results: High hypoxia levels (HLs) were found in 29% of pts., and low – in 71% of pts. Strong nuclear expressions of HIF-1 α were found in 7%, moderate – in 80%, and weak – in 13% of pts. Strong MVDs were observed in 54% and moderate – in 46% of pts. It was revealed a close association of HL in tumor both with expression of HIF-1 α in tumor cells ($P < 0.01$) and MVD rate ($P = 0.02$). The HIF-1 α expression correlated with histological grade of tumor ($P < 0.05$). HL and MVD in tumor correlated with clinical stage ($P < 0.05$). It was shown that increased PME/PDE ratio in tumor may be associated with the early development of distant metastases. It was also shown that tumor cells in BM are detected in 40% of patients with M₀ stage. It was observed that tumor in patients with negative BM is characterized both by high MMP-9 activity and low level of hypoxia. At the same time tumor in patients with positive BM is characterized both by high activity of MMP-2 and high level of hypoxia. High tumor HL positively correlated with decreased overall survival ($P = 0.044$). For overall survival, HL and HIF-1 α expression were independently predictive in multivariate analysis for lymph-node negative patients.

Conclusion: Statistical analysis has indicated that PME/Pi and PME/PDE ratios as well as HIF-1 α expression in tumor tissue may be used as an independent prognostic factors of clinical outcome in patients with GC. It is supposed that hypoxic profile of tumor can be a favourable basis for the appearance of DTC and formation of distant metastases.

doi:10.1016/j.ejcsup.2006.04.120

P61. PECULIARITIES OF GASTRIC CARCINOMAS IN PATIENTS UNDER 50 YEARS OF AGE

C. Schildberg, T. Horbach, S. Merkel, T. Papadopoulos, A. Dimmler, W. Hohenberger. Erlanger, Germany.

Introduction: Primary gastric carcinomas more commonly appear in advanced age; the portion of younger patients with this (<50 years) is about 7–15%. To discover possible clinical and pathologic peculiarities between the two groups, our clinic's patients who were under 50 years of age were compared to patients who were over 50 ($n = 481$).

Materials and Methods: The study's time-frame spanned from 01/01/1994 to 12/31/2002. The younger-aged group (median age 44 years) was composed of 73 afflicted patients; the older-aged group (>50 years) was composed of 408 operated patients (median age 68 years).

Results: Younger patients reported symptoms preoperatively more often than older patients (99% vs. 92%, $p > 0.05$). The diffuse gastric carcinoma predominated the younger collective of patients (82% vs. 49%, $p = 0.0001$). In differentiating the tumor stages, there were minimal differences between the two groups ($p > 0.05$). Postoperative complications in the sense of insufficient anastomoses was remarkably higher in older patients (5%) as compared to younger patients with 1% ($p = 0.22559$). There were remarkable differences in survival (5-year survival rate) in favor of the younger patients even after statistical age corrections were performed (54.1% vs. 41.1%; $p = 0.0414$).

Conclusion: In younger patients, the diffuse type predominates, which could point to differences in genesis. It is often only initially found in a late stage (IV) and is always associated with clinical symptoms. The treatment results in younger patients are more favorable than in the >50 group, not only in the view of the surgical complications, but also in lethality and 5-year survival. This is also true in consideration of the different life expectancies and gender differences.

doi:10.1016/j.ejcsup.2006.04.121

P62. SEMI-QUANTITATIVE GENE EXPRESSION PROFILING FOR THERAPY PREDICTION IN A BREAST CANCER NEOADJUVANT THERAPY STUDY APPLYING DOCETAXEL/EPIRUBICIN/ CYCLOPHOSPHAMIDE (TEC)

U. Vogt, C.M. Schlotter, U. Bosse, U. Bonk, B.H. Brandt. European Laboratory Association, Ibbenbueren, Germany; Clinical Centre, Ibbenbueren, Germany; Institute of Pathology, Osnabrueck, Germany; Institute of Pathology, Bremen, Germany; Institute of Tumor Biology, Hamburg, Germany.

Background: Currently there are no tests to assist in selecting the optimal preoperative chemotherapy (PST) regimens for breast cancer patients. Primary study goals are pathologically confirmed tumour response and the rate of breast conserving therapy. Secondary study goals are to find histopathologic and gene profiling patterns best correlating with tumour remission in a TEC based neoadjuvant setting as well as to evaluate cytostatic toxicity and quality of life.

Methods and Patients: In this neoadjuvant phase II study of totally 40 eligible patients with histologically confirmed invasive breast cancer Human Genome Survey Microarray (HGSM) expression profiling is preformed on jet-biopsy sample basis. The protocol was elaborated for the treatment of breast cancer patients suffering from a primary tumour greater than 1.5 cm or