Oncogenetics

P1

P53, Bcl-2, TS, TP, P-gp and Topo II alpha expression in hepatocellular carcinoma patients: association with clinicopathological findings

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Hepatocellular carcinoma (HCC) is one of the leading causes of cancer death in the world. As HCC is typically resistant to most cytotoxic agents; therefore it is important to determine expression patterns of important chemotherapy targets and their relation to clinicopathological features of patients. In this respect, we decided to evaluate the expression of p53, Bcl-2, P-glycoprotein, Topo II alpha, TS and TP proteins as important molecular markers in HCC and their relation to clinicopathological features of patients. Out of 40 surgically resected liver tumors from 3 different university hospitals during the years 2000-2003, 13 tumor samples were diagnosed as HCC. They were analyzed by immunohistochemical techniques using corresponding primary antibodies and LSAB2 detection kit. The highest prevalence of expression was P-gp with 76.9% and p53 with 70% of expression and the lowest one was Topo II with 42.6% of expression. The expression of Bcl-2 was also 55.6%. TS and TP staining were not observed in tumorous parts of biopsy samples. A significant correlation were observed between p53 expression and tumor cell differentiation (p=0.023). This data support the hypothesis that the p53 mutations may closely associated with tumor progression. Bcl-2 expression was significantly correlated with sex in our samples (p=0.09), that means all of our positive cases were males. P-gp negative expression was significantly correlated with age (p=0.022). No associations were observed between expression of Topo II and clinicopathological features of patients. High expression of P-gp, low expression of Topo II and Bcl-2 in studied tumor samples, may significantly affects successful chemotherapy in such patients. On the other hand, age and sex of patients could also affect the expression of these markers which can affect therapeutic outcome and disease prognosis. High intensity of TS and TP in non tumorous parts of the samples may suggest these markers as helpful parameters in distinguishing between hepatocellular tumors and other hepatic cells. Present results further emphasizes on the importance of these markers as valuable prognostic or predictive markers in clinical settings.

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Biological features familial and sporadic breast cancer

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Breast cancer (BC) is the most common cancer affecting women and the incidence rate of this cancer has risen in the Ukraine with an annual incidence of 59, 5 per 100,000 women in 2004. Basing on the statistics many investigators only 5–10% of BC cases are hereditary and germline mutation in the BC predisposing genes BRCA1 and BRCA2 may account for 60–90% of the hereditary cases and often at a younger age. The aim of this study is to identify clinical, morphological features of sporadic and familial BC.

Methods: We performed analysis of BC patients with familial breast cancer (69 patients – group A) and sporadic breast cancer (84 patients – group B) of Institute oncology of AMS of Ukraine. Clinical-genealogical, clinical, morphological and immunohistochemistry methods was used.

Results: According clinico-genealogical analysis revealed that 69 probands had 284 relative a first degree relationship and 641 – a second degree relationship. Out of them 33 had a mother with BC, 28 had a sister with BC. And 4 had both a mother and a sister with BC. In our study the patients with familial predisposition were predominantly of younger age. Mean age was 34,7±0,7 years in group A and 54,5±1,0 years in group B. The member patients continuing to menstruate at diagnosis was significantly greater in group with the familial BC in comparison with the sporadic BC and being 68,72% and 57,32% respectively. Year of occurrence of a tumor at the daughter which mother had BC, was much less, than at mother, and made 41±0,3 and 51,8±07 years accordingly. As a tumor morphology demonstrated a trend towards infiltrative tubular and lobular BC (89,3%), other types being encountered much less frequently (10,7%). In the sporadic BC group – 67,7% and 32,3% respectively. Tumors in group of family history exhibited high grade of malignancy, had a greater degree of nuclear pleomorfism, less tubule formation and previously negative for estrogen and progesterone receptors. There were no differences between patients with family and sporadic BC with respect to blood group, rhesus factor, pregnancies, childbirths, abortons.

Conclusion: These data suggest that phenotype of family BC seems to be more heterogenous and producibly distinguishable from sporadic BC. The addition of tumor morphologic particularity to the clinical profile might assist in better selecting individuals for BRCA mutation testing. And at last the particular attention should be focused on women who have a sister in whom BC was diagnosed under age 40 or less.