

P8a

Serum trace elements and the oxidation status in bladder cancer

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Introduction: A relatively wide range of trace elements are known to play important roles in biological processes, including the oxidative processes. There is epidemiologic evidence of the role of oxidative reactions in cancer induction especially bladder cancer, and most of these reactions result from imbalance of trace elements in the cellular structure. Manganese (Mn) plays an important role in antioxidant defenses and forms part of a Mn-dependent superoxide dismutase enzyme. Iron (Fe) is an essential trace element that is crucial to normal cell functioning and its deficiency is associated with several disease states. On the other hand, Chromium (Cr) is a short-lived oxidative metal in the cells. Zinc (Zn) is another trace element that increases in various oxidative stress states and may play an important role in cancer etiology. In the present study, the concentration of Fe, Cu, Zn, Cr, Mn, malon-dialdehyde (MDA) as a biomarker of lipid peroxidation and total anti oxidant capacity (TAC) as an anti oxidant marker, were determined in the serum of patients with bladder cancer in comparison to healthy subjects.

Materials and Methods: This cross-sectional study was conducted on 51 patients with bladder cancer and 58 healthy volunteers after age, sex, and smoking habits were matched. After overnight fasting, samples were collected. The concentrations of Fe, Cu, Zn, Mn and Cr were measured by atomic absorption spectroscopy, plasma antioxidant status was evaluated using FRAP assay and MDA was measured according to procedure of Ohkawa et al. Comparisons were made using Student's t test.

Results: There was a significant increase in mean Cu and Cu/Zn serum level in bladder cancer patients compared to the control group (p value <0.001). In contrast, the serum Zn level in patients having bladder cancer was significantly lower than in the control group (p value <0.05). Moreover, the serum Fe level was significantly lower in the patients than the control group (p value <0.001). Serum concentration of MDA (p value <0.001) and Cr concentration (p value <0.05) were significantly increased in patients with bladder cancer. There was a significant decrease in serum concentration of Mn (p value < 0.001) and TAC (p value <0.001) of patients in comparison with healthy participants.

Conclusions: In the present study, a relationship was seen between the level of trace elements and the occurrence of bladder cancer, suggesting that an increase in the serum level of Cu and Cr and a decrease in the levels of Zn, Fe and Mn might be important causes of bladder cancer occurrence; however, defining such a cause-and-effect relationship needs several prospective studies to be done, which seems necessary with regard to the high prevalence of this cancer. In addition, regarding the findings of the study, we suggest that a diet rich in anti oxidants, Mn, Fe and Zn and low in Cr and Cu, and also controlling and lowering the ambient standard for Cr in the environment, may have some more protective role in preventing bladder cancer.

Lifestyle, Genetics

P9

Clinical features and prognosis of hereditary breast cancer

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Background: Breast cancer (BC) is the most prevalent malignant tumor in women in developed countries. According to the data of the National Cancer Register, in 2007 the morbidity rate in Ukraine was 61.2 per 100,000 women. Hereditary BC comprises 10–15% of overall BC incidence. The aim of our investigation is to identify clinical, morphological and immunohistochemical features of hereditary BC.

Methods: clinico-genealogical, morphological, immunohistochemical analysis and statistics.

Results: Based on clinico-genealogical analysis, the groups of the patients with hereditary and sporadic BC were delineated. The tumor associations in families of patients with hereditary BC were such as follows: mammary glands – 51.0%, ovary – 21.6%, gastric – 17.6%. It was established that in patients with hereditary BC, exogenous and endogenous risk factors (number of abortions, early menarche, age at pregnancy, number of births, duration of lactation period, smoking, breast injury, and body weight) are of relatively less importance in cancer development than in sporadic BC. Hereditary BC is more common in patients with dys hormonal hyperplasias of the breast. Based on the clinical features, hereditary BC is characterized by smaller size of tumours – 1.5 ± 0.6 cm, while being more malignant (high histological grade) and with worse prognosis. Hereditary BC is characterized by absence or low level of the expression of estrogen and progesterone receptors and BRCA1 protein. The overall survival in patients with hereditary BC was significantly poorer than in patients with sporadic BC (3-year survival rate, 72.42% and 88.06%, $p=0.02$; 5-year survival rate, 52.6% and 80%, $p=0.02$; 10-year survival rate, 15.8% and 26.7%, accordingly).

Conclusion: The results of complex examinations may be introduced to the practice of oncological clinics for delineating groups of patients with hereditary BC for their monitoring, which would be advantageous for early BC detection.

P10

Age-dependent derepression of transposons as common cause of ageing and cancer

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Apparently, a specific set of microRNAs and piRNAs expressing in stem cells can restore initial profile of their epigenetic markers through RNAi-directed DNA methylation, thus pluripotent immortal status of these cells is supported for ever and minimal level of the transposons activity is achieved. However, cell differentiation, starting with the most early stages, must be accompanied with repression of genes of some microRNAs from the primary set, otherwise these microRNAs would prevent expression of the stage-specific genes. As a result, differentiating cells can lose slowly the repressive chromatin markers with time, and this will excite the derepression of silent transposons and other mobile elements, therefore increase of DNA damage induced by them, and following activation of cell DNA repair system including mechanisms based on homologous recombination. In our opinion, these mechanisms cause not only the DNA repair, but also unauthorized recombinations

in the telomere capping structures, since they are pre-recombination structures. As a result, the T-loops converse into rings and, accordingly, telomeres are shortened for the length of the lost circled DNA (50–500bp) that exceeds few times DNA loss over the end-replication problem (3–5bp). This process can cause quick exhaustion of one or more cell telomeres and, therefore, following apoptosis of cells, in which the illegitimate activation of recombination process becomes apparent, and which can be transformed through transposons activity. Thus the telomere length is usually genomic stability indicator.

Normal cells, e.g. lymphoid cells, in which DNA recombination must take place at the certain development stages, protect own telomeres from exhaustion during these stages through the telomerase activity increasing. However, some transformed cells can escape the telomere shortening through telomerase hyperexpression or ALT-mechanism and form tumour.

Apparently, large quantity of organism cells reaches with age the threshold of illegitimate activation of silent mobile genomic elements. Following apoptosis of most of these cells causes the ageing as biological phenomenon, while the transposon-mediated transformation and surviving of part of them determines correlation between ageing and cancer appearance. Otherwise, derepression of latent mobile genomic elements should be facilitated due to disruption of links between nuclear lamina and chromatin, particularly in Hutchinson–Gilford progeria syndrome.

P11

Metabolic syndrome as modifiable risk factor in breast cancer

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Introduction: Hypercholesterolemia, hypertriglyceridemia, insulin-resistant diabetes and hypertension set up the Metabolic Syndrome scenario and often coexist with overweight or obesity. Metabolic Syndrome represents a condition prone to the onset of hormone-related tumours. Although there is no chance to carry out an effective primary prevention, it could be useful to reduce the weight of modifiable risk factors of breast cancer (high BMI and Metabolic Syndrome), through life-style adjustments such as low-calorie diet and physical activity.

Materials and Methods: Our study is a case-control one. Cases are represented by women with history of breast cancer, controls are constituted by healthy women, women with familial history of BC and/or women with diagnosis of border-line lesions. During routine clinical-instrumental controls, weight and height have been measured, arterial pressure and venous blood samples have been taken from each woman. BMI has been calculated as weight indicator. Analysis on arterial pressure values and biochemical results regarding glycaemic and lipidic metabolism got from blood samples have been used for Metabolic Syndrome diagnosis. Presence of at least three of the previous described metabolic alterations has been considered diagnostic for Low Grade Metabolic Syndrome, four or more of those alterations for High Grade Metabolic Syndrome. Association between these elements and breast cancer risk calculation have been performed by the means of χ -squared test and logistic regression analysis (OR 95% CI).

Results: Our current survey includes 195 cases and 351 controls. 75.1% of all women is free from any metabolic disease, 15.6% is affected by three disorders (Low Grade

Metabolic Syndrome), 9.3% is affected by four or more disorders (High Grade Metabolic Syndrome). Especially in the High Grade Metabolic Syndrome group (9.3%) there is a difference, although not statistically significant, between cases (12.3%) and controls (7.7%) respectively ($p=0.2$). OR confirms this trend for the Low Grade Group 1.04 (95% CI 0.64–1.69) and for the High Grade Group 1.69 (95% CI 0.94–3.05).

Conclusions: Metabolic Syndrome seems to play an essential role in breast cancer onset. Our goal is to implement the National Cancer Institute survey to establish statistically significant differences between cases and controls and to improve research in breast cancer primary prevention.

P12

Smoking during the period of time between menarche and first childbirth and breast cancer morbidity

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Numerous factors are associated with breast cancer risk. Among nonmodifiable risk factors early age at menarche and late age at first birth belongs to the group of mostly quoted. Modifiable risk factors are associated with life style. Cigarette smoking is one of these risk factors. However epidemiological and experimental works show the association between smoking and breast cancer development, no direct link has been found. The reason why early age at menarche and late age of first birth play a role in breast cancer also needs to be explained.

Material and Methods: Self made questionnaire consisting of 19 questions was the tool used in our study. 150 women with histopathologically proven breast cancer were included in the study. The age range of tested women was 35–78 years. 4 of them had incompletely filled questionnaires and were excluded from the study. So final number of responders was 146. Women were asked specific questions, about their reproductive history, smoking, time and duration (especially of smoking during the time between menarche and first childbirth) and history of their suffering from breast cancer. Analyses were performed by using STATISTICA software.

Results: There is no statistically significant difference between groups of smoking and never smoking among women suffered from breast cancer (71 and 76 cases respectively). 48 of women from smoking group smoked during the time between menarche and first childbirth.

Conclusion: Smoking during the time between menarche and first childbirth augment risk for breast cancer morbidity need take into consideration.

P13

Educating women in a resource poor area in breast cancer awareness. A pilot study of psychological consequences

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Introduction: The name cancer awareness and screening in resource poor, illiterate population has a significant psychological impact on both the people and society. To aware and screen about this disease specially breast cancer require access to a range of practical supports during survey and improve health outcomes. This study aims to map the psychological and practical support need of Thar Desert of India population in remote area. To date no research has explored the unmet needs of awareness in this resource poor