Introduction: It is well known that course of metastatic disease is influenced by different parameters than primary breast cancer. In that context the prognosis of metastatic breast cancer patients is not easily predicted. Aim of this study was to determine the influence of selected biomarkers on different time dependent sequences of follow up i.e. relapse-free survival (RFS) and overall survival (OS) in metastatic breast cancer.
Material and Methods: This study included 109 metastatic breast cancer patients with visceral/nonvisceral involvement (median age 50 years) with known clinicopathological characteristics. HER2, Topo2a and c-myc amplification was determined by chromogenic in situ hybridization (CISH) on the same paraffin embedded primary tumor samples. Different types of chemotherapy and/or endocrine therapy were administered to the majority of the women in adjuvant and metastatic setting. RFS was defined as time from diagnosis till appearance of metastatic disease and OS was defined as time from diagnosis till death. RFS and OS were estimated using the Kaplan Meier method and survival differencies were compared with the log-rank test. P value less than 0,05 was considered as statistically significant.
Results: Only HER2 amplification was predictive for RFS</= 24 months (p<0,04) but not for RFS >24 months, whereas Topo2a amplification, as well as estrogen receptor and progesterone receptor status were associated with OS (5 year survival) (p=0,001, p=0,012 and p=0,003, respectively). Amplification of c-myc was not relevant neither for RFS and OS. In addition, among clinicopathological parameters, nodal status, the number of lymph nodes at the time of diagnosis and tumor size were relevant for RFS </=24 months, while age, menopausal status, stage and tumor size were relevant for OS up to 5 years.
Conclusion: These findings are consistent with the hypothesis that biologic factors of the initial primary tumor indeed are associated with relapse-free and postrelapse survival, and that the prognosis in breast cancer is determined strongly by intrinsic molecular characteristics of the primary tumor. Our results indicate that relevance of amplification of the selected genes regarding clinical outcome, change over time, meaning that some biomarkers have significant role earlier during the progression of disease and the biological effect of the other biomarker could be delayed. Determination of designated molecular biomarkers such as amplifications of different genes at the time of primary diagnosis, concomitantly with clinicopathological parameters could help and improve decision making in regard to the treatment of patients.

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IMMUNE REACTIVITY IN PATIENTS WITH BREAST CANCER ASSOCIATED WITH TYPE 2 DIABETES MELLITUS

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Immune reactivity of patients with early or advanced breast cancer, associated with type 2 diabetes mellitus, compared with healthy controls, has been measured using in vivo and in vitro tests. The results of our study show that impairment of cellular responsiveness occurred in women with advanced disease.
The immunological indices were studied by immunocytochemical procedure in 56 patients with breast cancer, associated with type 2 diabetes mellitus. The levels, ratio and phenotypic patterns of peripheral blood T-cells were assessed in patients with primary tumors vis-a-vis biological pattern of tumor, stage, rate of growth, locally-regional extension, pathogenetical type of tumor and such breast cancer-related physiological characteristics as age and menstrual function. It was found that immunodepression in breast cancer patients can be detected by laboratory examination at stage IIb. It may manifest itself in a changed ratio of main subpopulations of T-lymphocytes, decrease in the total level of T-cells and increase in dysfunctional ones. The worst immunological indices were identified in patients younger than 35 and those with rapidly growing tumors. Pronounced immunosuppressive condition has been discovered along with amount decrease of T-lymphocytes CD3, CD8, CD4, B-lymphocytes and CD4/CD8 factor, as well as content malfunction of IgA, IgG, IgM and CIC. But we found an increased of total CD16 lymphocytes which correlated with CD19 membrane receptors more expressive at patients with diabetes mellitus.
A correlation was made between the complex of metabolic indices (the concentration of free fatty acids, cholesterol, beta-lipoproteids and triglycerids in blood) and the complex of immunological indices (the number of T-lymphocytes by clone determinants) in healthy females of two age groups and in breast cancer patients. There were examined 20 healthy females aged 18-29, 19 healthy females aged 40-78 and 56 primary breast cancer patients, and also 30 patients and their age was analogous to that of the second control age group. It was stated that healthy females with age show a parallel worsening of metabolic and immunological indices (the correlation coefficient being equal to -0.57 and -0.56 accordingly (P less than 0.01 and P less than 0.02) that corresponds to the phenomenon of metabolic immunodepression which manifested by diabetes mellitus. The same phenomenon is observed in breast cancer patients (r = 0.42, P = 0.02). Contrary, in primary patients associated with type 2 diabetes mellitus despite analogously decreased immunity the correlation coefficient was -0.23. Consequently, the mechanism of immunosuppressive effect of the tumor seems not to be related to the changed concentration in blood of the indices under study.

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FACTORS AFFECTING CHANGES IN IMMUNOHISTOCHEMISTRY PHENOTYPE OF BREAST CANCER

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Background: Modern clinical trials indicate that during system treatment change of breast cancer phenotype is observed quite often.
Aim: The aim of work was research of frequency of changes and factors that influenced on the changes of immunohistochemistry (IHC) status of tumor in the process of treatment and initiation.
Material and Methods: Clinical data of 65 patients with breast cancer was analyzed. The age of patients was between 29 to 73 years at the time of primary diagnosis. Primary and continual IHS investigations of tumors were undertaken in all cases.
The molecular types of breast cancer were presented thus: 32 patients initially had luminal A type, luminal B type was determined in 17 women, 7 cases with triple negative IHC-status and 9 clinical supervisions with overexpression of epidermal growth factor.
Results: There is a high level of IHC-status' changes in the process of tumor development and treatment: frequency of changes of breast cancer immunophenotype was 44.78%.
Conducted a cross-correlation and regressive analysis allowed to find the next conformities: the change of IHC-status is expected for patients with luminal B type of breast cancer, in cases, when the values of steroid receptors are near to negative and Her-2 equals 2+; for women in reproductive age, with low-lever differentiated carcinoma; in case of receiving target and radiation therapy during previous treatment. For patients with a recurrent type of breast cancer also the presence of endocrine therapy in anamnesis is important.
The study of frequency and features of conversion of biological aggressiveness of tumor will allow to optimize tactics of treatment and improve a prognosis.

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INCREASED RELAPSE RATIOS IN NODE-POSITIVE BREAST CANCER PATIENTS WITH METHYLENETETRAHYDROFOLATE REDUCTASE POLYMORPHISM

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