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Immunocytochemical study of p-53 and HER-2 expression in FNA specimens from breast cancer patients

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Background: A prospective study for the prognostic value of the immunocytochemical identification of p-53 and HER-2 at the FNA cytology of the primary tumors of patients withbreast cancer. An attempt to evaluate the correlation of the p-53 and HER-2 expression with the infiltration of the ipsillateral axillary lymph nodes (LN).

Methods: We applied immunocytochemistry at the FNA specimens of the primary tumor (tumor size until 3cm) of 224 breast cancer patients and clinically negative axillary LN for the identification of p-53 and HER-2. These patients consequently underwent modified radical mastectomy or breast-conserving surgery and standard axillary dissection of level I and II at the Metaxa Memorial Anticancer Hospital. Then we examined histologically the presence or not of ipsillateral LN metastasis in every case.

Results: The median age of these patients was 52.8 years (32–82 years old). 97 patients had free (negative for metastatic infiltration) LN, whereas 127 had at least 1 positive LN. Among the patients with positive HER-2 at the FNA (88 patients) the 65 (73.86%) presented an infiltration of at least 1 LN, whereas only the 45.58% of the 136 patients with negative HER-2 (p-value<0.001). As far as the p-53 was concerned 31 (67.39%) of the 46 patients with positive p-53 and 53.93% of the 178 patients with negative p-53 had LN invasion (non significant). 30 of our patients (13.39%) presented a simultaneous positiveness for p-53 and HER-2 and 26 of them (86.66%) had infiltrated LN (p-value < 0.001).

Conclusions: Tumors with positive p-53 and HER-2 express an aggressive behaviour. The preoperative evaluation of these two biological markers at the FNAs of patients with breast cancer could assist for the better therapeutic plan and prognosis of the disease.

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The role of tumor markers in breast cancer recurrence

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The aim of the present study was to evaluate the clinical performance of tumor markers in breast cancer recurrence. One hundred and seventy-four breast cancer cases were entered into the study and followed up for 132 months (mean=34.0, SD=28.0). The mean age of the patients at diagnosis was 47.1 (SD=12.3) ranging from 23 to 81 years. Most patients (51%) presented with stage II breast cancer. 81% of the patients underwent modified radical mastectomy and the remaining 19% had breast preservation surgery. Recurrence occurred in 22% of patients during the follow up time. The association between clinical recurrence with age, tumor size, nodal involvement, stage, type of surgery and pathology, serum CA15.3, CEA, P53, ER, PR, and HER-2 status were examined by using the forward conditional logistic regression analysis. The results indicated that recurrence was significantly predicted by the existence of CA15.3 (odds ratio = 6.1, 95% CI = 1.62–23.1, P=0.007). The findings showed that independent of age and other know prognostic factors; CA15.3 is a significant predicting factor for recurrence in breast cancer patients.

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Expressions of O (6)-methylguanine-DNA methyl transferase MGMT and p53 in breast cancer

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Background: MGMT is one of the DNA repair protein. It is reported that MGMT is a strong predictor of survival in brain tumors and that mutant p53 protein might be associated with down regulation of MGMT expression in brain tumor.

Purpose: This study investigated the expression s of both MGMT and p53 in breast cancer to clarify the correlation between MGMT and p53 expression.

Methods: Using immunohistochemical staining with an anti-MGMT and anti-p53 antibody, the MGMT and p53 expressions in tissues from 48 consecutive cases of primary breast cancer patients was examined. From the correlation between MGMT and p53 expression and the clinicopathological findings, the prognosis for survival were analyzed.

Results: The expressions of both MGMT and p53 were classified as negative or positive on the basis of staining. The specimen which had negative MGMT expression showed significantly higher expression of p53 (p=0.026, Chi-squared test). No relationship between MGMT expression and each of clinicopathological findings was identified. However, a relationship of negative staining of p53 and estrogen receptor expression was observed. The prognosis of the patients with negative staining of MGMT was worse than that of other patients. The prognosis of the patients with positive staining of p53 was worse than that of other patients.

Conclusions: The p53 protein might be associated with regulation of MGMT expression in breast cancers. MGMT immuno-negativity and p53 immuno-positivity migit be strong predictors of survival in breast cancers.

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Association between pS2 and cathepsin-D in breast carcinoma: biological and clinical aspects

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From the biological point of view our aim was to define estrogen-regulated versus nonestrogen-regulated pS2 and cath-D expression and, then, to examine the association between estrogen-regulated pS2 and cath-D in relation to pT and pN status of carcinomas. From the clinical point of view, our aim was to define high risk subgroups of breast cancer in relation to cath-D expression. This study included 152 patients with histologically verified breast carcinoma. ER and PR were assessed in accordance with recommendation of EORTC. pS2 and cath-D were determined using immunoradiometric assay. The results were analysed using non-parametric statistical methods. Estrogen-regulated cut-off value for pS2 was defined on the basis of the ER-status- and histological grade-, as well as menopausal-related pS2 quantitative values. No overlapping of pS2 protein values was obtained between ER-positive and ER-negative carcinomas within postmenopausal subgroup with histological grade II and within pre- and postmenopausal subgroups with histological grade III. The highest pS2 protein level observed in ER-negative subgroups was considered as the cut-off value (15 ng/mg). Estrogen-regulated cut-off value for cath-D was defined on the basis of the ER–PR status-, auxiliary lymph node- and tumor size-related cath-D quantitative values. No overlapping of cath-D protein values was obtained neither between pN0 and pN+ nor pT1 and pT2/3 carcinomas within ER, PR-negative subgroup. The highest cath-D protein level observed in ER, PR-negative TN-stage favorable subgroups was considered as the cut-off value (28 pmol/mg). Our further analysis aimed at examination of pT- and pN-related association between estrogen-regulated pS2 and cath-D expression. A statistically significant association was only obtained in pT1 carcinomas. Evaluation of disease free interval in the first three years, among patients bearing pT1 carcinomas, showed a statistically significant difference between estrogen-regulated and nonestrogen-regulated cath-D expression. An unfavorable course of disease was observed in patients with carcinomas expressing estrogen-regulated cath-D. From the biological point of view it is important to point out that the positive association of estrogen-regulated pS2 and cath-D expressions is an early biological event occurring in pT1 carcinomas. Moreover, the estrogen-regulated cath-D defines high-risk subgroup within generally accepted low-risk pT1 breast carcinomas group.

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Expression of multidrug resistance associated genes MRP1, MRP2 and MRP3 in primary and anthracycline exposed breast cancer

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Introduction: Multidrug resistance (MDR) associated proteins MRP1, MRP2 and MRP3 confer in vitro resistance to a wide range of drugs. We investigated their possible role in clinical breast cancer resistance to anthracycline-based chemotherapy.

Methods: Using real-time reverse transcriptase polymerase chain reaction (RT-PCR) and immunohistochemistry (IHC) the expression of MRP1–3 was quantified in nine breast cancer cell lines and 30 breast carcinoma samples.

Results: Detectable levels of MRP1–3 mRNA were present in all breast cancer cell lines and tumor samples. No increase of expression was detected between primary untreated carcinoma samples and samples taken after neoadjuvant anthracycline treatment. IHC was not suitable for