

VIII. İNGİLİZCE ÖZET

THE INTERACTION OF GLUCOSE TRANSPORTER 1 AND MAST CELL TRYPTASE LEVELS WITH PROGNOSTIC AND PREDICTIVE FACTORS IN EARLY STAGE BREAST CANCER

SUMMARY

Purpose: Identification of prognostic and predictive factors is critically important in early stage breast cancer due to the chance of achieving cure with appropriate adjuvant treatments. Major prognostic and/or predictive factors include lymph node metastasis, size and estrogen receptor (ER) and progesterone receptor (PR), human epidermal growth factor receptor-2 (HER2/neu), Ki-67 and p53 status of the primary tumor, the age, performance and menopausal status of the patient. Mast cell tryptase (MCT) is a trypsin like enzyme with serine peptidase (proteinase) activity. This enzyme's activity regulates tumor blood flow as well as oxygenization and supports tumor growth and metastasis by promoting angiogenesis. Glucose transporters (GLUT) family, represent a group of trans-membrane proteins that have a role on internalizing glucose in the cells. GLUT-1 is one of the most common and widely studied subtype of the GLUT family. Consumption of glucose increases in malignant cells due to the accelerated cell metabolism. The prognostic value of both MCT and GLUT-1 expressions in early stage breast cancer has not been established well. The purpose of this study was to measure the levels of MCT and GLUT-1 expressions in early stage breast cancer patients operated in our hospital and to determine the interaction of these parameters with established clinical and pathological prognostic and predictive factors.

Methods: We studied the hospital registries and mastectomy or lumpectomy materials of 35 postmenopausal women that have been operated in-between the years 2003-2008 for breast cancer and referred to the Department of Pathology of Adnan Menderes University, Medical Faculty. The patients with histories of addiction and use of medicine, neoadjuvant treatments or co-morbid diseases to interact with the study parameters were excluded. The breast tumor materials stained with routine hematoxylin & eosin (H.E.) were also analyzed by immunohistochemical methods for ER, PR, HER2/neu, GLUT-1, and MCT expressions. The statistical analyzes were performed by *SPSS Windows version 14.0* PC packet program and Fisher's Exact, Mann Whitney U, and Kruskal Wallis tests and Pearson's and Spearman

correlation analyzes were used as needed. Statistical value of $p < 0.05$ was accepted as significant.

Results: The patients' mean age of diagnosis was 64 ± 11 years. Lymph node metastases was positive in 19 (54%), and negative in 16 (46%) patients and the tumor size was at T1 and T2 stages in 80%. The cell type was invasive ductal carcinoma in 24 (69%), ER and/or PR was positive in 28 (80%), and HER2/neu was positive (3+) in 11 (31%) patients. The correlations were positive in-between the prognostic and predictive factors such as; lymph node status and tumor size, pathological stage and nuclear grade; tumor size and pathological stage and nuclear grade; pathological stage and nuclear grade; nuclear grade and histological grade; and ER and PR. These results did not also differ in the subgroup analyzes of the invasive ductal carcinoma cases. The MCT levels and GLUT-1 expressions were negative in 5 (14%) and 11 (31%) patients, showed varying degrees of positivity in 30 (86%) and 24 (69%) patients, respectively. In study patients with positive MCT activity there was a positive correlation in between the grade of fibrosis and MCT activity. Also, the MCT activity had a significant negative correlation with histological grade. There was no significant correlation in-between the GLUT-1 expression level and the prognostic and predictive factors as well as the existence of diabetes mellitus and the body mass index of the patients. In the subgroup analyzes of the 16 (46%) low risk patients with negative lymph node metastases, GLUT-1 expression level showed positive correlation with primary tumor size, however, this correlation did not reach to significant levels.

Conclusion: The determination of correlations in-between MCT activity levels and tumor fibrosis and histological grade in the overall study group; and in-between GLUT-1 expression levels and primary tumor size in the node negative patients subgroup in this study suggest that, both MCT activity and GLUT-1 expression levels might have prognostic values in early stage breast cancer patients and should be further researched in extended prospective studies with longer follow-up periods.

Key Words: Breast cancer, prognostic factors, mast cells, tryptase and GLUT-1.

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