The presence of NOD2 mutation in younger breast cancer patients – single center experiences

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Introduction: The population risk of breast cancer before the age of 50, associated with the NOD2 mutation, is approximately 1%. It increases 5 times the risk of DCIS <50 years. The purpose of this study was to evaluate the presence of NOD2 (c.3016_3017insC) mutation in younger breast cancer (BC) patients (<45 years) according to clinicopathological factors in comparison to control group.

Material: We have analyzed prognostic factors in younger BC patients with confirmed NOD2 (c.3016_3017insC) (n=42) mutation. Control group was selected from BC patients without tested mutations (n=392). The presence of the most common mutations in BRCA1 (c.68_69delAG, c.181T>G, c.4034delA, c.3700_3704del5), BRCA2 (c.5946delT and c.9403delC), CHEK2*1100delC or I157T mutations genes were excluded. Mutation analysis was carried by a multiplex allele-specific polymerase chain reaction assay.

Results: The median age at breast cancer diagnosis for the carriers of the NOD2 mutation was 47 years (from 27 to 68) and for control group 53 years (from 26 to 78). 51 patients were in age under 45 years: 16 (38%) in NOD2 mutation carriers and 42 (22%) in control group, p=0.040. Gastrointestinal cancers in family history (31% vs. 7%, p=0.012), especially colorectal cancer (13% vs. 1%, p=0.061) were reported more frequently in patients with NOD2 mutations. There was also observed tendency to the presence of breast cancer in family history in NOD2 mutation carriers (19% vs. 9%, p=0.369) (age <45 years). In group of patients in age >45 years cancers in family history, including breast cancer were observed more often in NOD2 mutation carriers in comparison to control group of patients (73% vs. 31%, p=0.0001, for breast cancer in family history: 42% vs. 10%, p=0.0001).

HER2 overexpression was reported significantly more often in control group (51.1% vs. 6.3%; p=0.007). In contrary, there was no differences between NOD2 mutation carriers and control group according to ER (31% vs. 40%, p=0.587) and PR (38% vs. 43%, p=0.787) negative steroid receptor status. Breast cancer subtype A was more frequent in NOD carriers compared to control group (38% vs. 7%, p = 0.003). Lower histological grade G1-G2 (56% vs. 68%, p=0.395) and lymph nodes without metastases (69% vs. 48%, p=0.174) were observed similarly frequently in NOD2 mutation carriers than control group.

Conclusion: The presence of NOD2 mutations (in age <45 years) were associated with younger age of disease diagnosis and history of gastrointestinal cancer in family. Breast cancer in family history was characteristic for NOD2 mutation carriers in age>45 years. Luminal A breast cancer subtype was most characteristic for this group.