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 were 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.5266dupC, 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.