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TP53 Mutations in Molecular Subtypes of Breast Cancer in Young Pakistani Patients

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Abstract : Background: The incidence and mortality of breast cancer vary significantly in geographically distinct populations. In Pakistan, breast cancer has shown an increase in incidence in young females and is characterized by more aggressive behavior. The tumor suppressor TP53 gene is a crucial genetic factor that plays a significant role in breast carcinogenesis. This study investigated the TP53 mutations in molecular subtypes of both nodes negative and positive breast cancer in young Pakistani patients. Material and Methods: p53, Estrogen Receptor (ER), Progesterone Receptor (PR), Her-2 neu and Ki 67 expressions were analyzed immunohistochemically in a series of 75 node negative (A) and 75 node positive (B) young (aged: 19-40 years) breast cancer patients diagnosed between 2014 to 2017 at two leading hospitals of Punjab, Pakistan. Tumor tissue specimens and peripheral blood samples were examined for TP53 mutations by direct sequencing of the gene (exons 4-9). The relation of TP53 mutations to these markers and clinicopathological data was investigated. Results: Mean age of the patients was 32.4 + 9.1 SD. Invasive breast carcinoma was the most frequent histological variant (A=92%, B=94.6%). Grade 3 carcinoma was the commonest grade (A=72%, B=81.3%). Triple negative cases (ER-, PR-, Her-2) formed most of the molecular subtypes (A=44%, B=50.6%). A total of 17.2% (A: 6.6%, B: 10.6%) patients showed TP53 mutations. Mutations were significantly more frequent in triple negative cases (A: 74.8%, B: 62.2%) compared to HER2-positive patients ($P < 0.0001$). In the multivariate analysis of the whole patient group, the independent prognosticator were triple negative cases ($P=0.021$), TP53 overexpression by IHC ($P=0.001$) and advanced-stage disease ($P=0.007$). No statistically significant correlation between TP53 mutations and clinicopathological parameters was found ($P < 0.05$). Conclusions: It is concluded that TP53 mutations are infrequently present in breast carcinoma of young Pakistani population and there was no significant correlation between p53 mutation and early onset disease. Immunohistochemically detected TP53 expression in our resource-constrained to set up can be beneficial in predicting mutations at the younger age in our population.

Keywords : immunohistochemistry (IHC), invasive breast carcinoma (IBC), Pakistan, TP53
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