Genetic mutation profile in HER2 positive lobular breast cancer

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BACKGROUND

HER2 positive lobular cancer is a rare subtype of breast cancer. Although clinical management remains similar between HER2 positive invasive lobular cancer (ILC) and invasive ductal cancer (IDC), there are variations in genetic mutations associated with them.

METHODOLOGY

We searched the cBioPortal and AACR Project GENIE databases for primary breast cancer cases. Among the available datasets, only those with reported HER2 positive status were included. Duplicate or multiple entries were sorted out by the patient and sample id provided in the database. The genetic mutations which were defined to be cancer causing based on OncoKB databases were only included in the study. The frequency of genetic mutations associated with HER2 positive ILC, HER2 positive IDC and HER2 negative ILC were expressed as percentage of total profiles sampled for the corresponding genes. The difference in frequency of common genes in the subset were evaluated with fisher exact test and reported with a p-value.

RESULTS

We found 58 cases of HER2 positive ILC, 753 cases of HER2 positive IDC and 652 cases of HER2 negative ILC. The most common genetic mutation in HER 2 positive ILC were CDH1(52.8%), PIK3CA(41.5%), and TP53(22.7%). While for HER2 positive IDC, TP53(60.9%) was the most prevalent mutation followed by PIK3CA (32.6%) and GATA3(9.2%). There was a statistically significant difference in the prevalence of TP53 mutations among HER2 positive ILC and HER2 positive IDC (p<0.001), but not with PIK3CA (p=0.23). Among the HER2 negative ILC cohort, the most common genetic mutations were similar to HER2 positive ILC: CDH1(67.6%), PIK3CA(49.1%) and TP53(12.6%). However, there was a statistically significant difference in the frequency of CDH1 mutations among HER2 positive and HER2 negative ILC (p=0.05).

CONCLUSION

Even though HER2 positive IDC and ILC are treated in a similar way, this study identifies that HER 2 positive ILC has a distinct genetic profile compared to HER2 positive IDC, and has more similarities to HER2 negative ILC. These findings suggest a need to identify targetable treatment options in women with HER2 positive ILC.

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