Research Article

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Prevalence of Breast Cancer Intrinsic Subtypes and Its Association with Clinico-Pathological Feature

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Abstract

Breast cancer is the commonest cancer in women worldwide and represents a highly heterogeneous group of tumours particularly in terms of molecular features, prognosis and response to therapy.

Breast cancer molecular classification can predict the prognosis of breast cancer in terms of recurrence and help and guide us regarding the treatment decision about systemic therapy. Breast carcinomas may be stratified into subtypes similar to those defined by Gene expression profiling using a panel of immune-histochemical (IHC) markers. Routine IHC evaluations of breast cancers may, therefore, provide a reasonable alternative to costly genetic assays especially in under-resourced healthcare systems. The purpose of this study is to investigate the prevalence of molecular subtypes and correlate it to clinic-pathological features.

Methods: *From 2005 to 2017 total of 4847 Breast cancer patients, in whom complete information was available to classify them into luminal subtypes were retrieved and classified into intrinsic subtypes and patients information in each type was collected about age, tumour size, stage, grade and nodal status.*

Results: *In luminal classification, a highly significant difference was found in mean age ($p<0.001$) tumour size ($p<0.001$), grade, metastasis and Ki67. The statistical significance of Her 2 positive and triple negative was found with stage, grade, metastasis and Ki67.*

Conclusions: *IHC assignment into Luminal subtypes is clinically informative in our patients and routinely using this in our practice could identify patients that may need a more aggressive treatment to reduce the likelihood of recurrences.*

Keywords: Breast cancer subtypes, ER, PR, Her2neu. Ki67

Introduction

Breast cancer is the commonest cancer in women worldwide and represents a disease with wide spectrum particularly in terms of tumour histology, biology, prognosis and response to therapy.

Breast cancer is characterized by cellular heterogeneity. Breast tumours with same size and histopathology can exhibit variable clinical presentations, disease behaviour and response to therapy. Analysis of gene expression profiling and immunophenotypic characteristics suggests that breast cancer is not a single entity but a heterogeneous disease [1,2].

The current classification of breast cancers is mainly based on morphology, which does not explain this difference in the outcome. Breast cancer molecular classification can predict the prognosis of breast cancer in terms of recurrence and help and guide us regarding the treatment decision about systemic therapy. Knowing this in the 8th edition of AJCC staging, molecular parameters have been given a significant place [3].

Breast carcinomas may be stratified into subtypes similar to those defined by gene expression profiling using a panel of immune histochemical (IHC) markers [4-6]. Therefore routine IHC evaluations of breast cancers may provide a reasonable alternative to expensive genetic assays especially in under-resourced healthcare systems. The purpose of this study is to investigate the prevalence of molecular subtypes and correlate it to clinic-pathological features.

Methods

From 2005 to 2017 breast cancer patients' data was retrieved from

purpose-built breast cancer software, where all the data about breast cancer patients is maintained. Total of 4847 breast cancer patients, in whom complete information was available to classify them into intrinsic subtypes were retrieved and classified into subtypes according to St. Galen's guidelines (Luminal Alike. Luminal B like, Luminal Her, Non-luminal Her2 and Triple negative) and patients information in each type was collected about age, tumor size (T), stage, grade and nodal status.

Statistical Analysis

Statistical Package for the Social Sciences Software (SPSS, version 21) was used for analysis. A quantitative variable such as age at diagnosis was reported as mean ±SD and student t-test was applied for comparison of mean differences. Qualitative variables as tumour size (T), metastasis, stage, grade, nodal status, Her2, Ki67, Hormone receptor and luminal classification were presented in terms of frequency and percentages and a chi-square test was applied to see the association between these variables. Furthermore, the binary logistic and multinomial logistic regression was applied to find odds ratios for significant variables. P value ≤0.05 were considered as significant in all analysis.

Results

Total 4847 patients were evaluated in the study. The mean age of patients at diagnosis was 49.76±12.58 as far as luminal classification is concerned, Luminal Alike was 18.3%, Luminal B like was 25.9%, luminal Her2 was 3.8%, Non-luminal Her2 was 16.3%, and triple negative was 25.7%. Her2 positive was found in 1459 (30.1%). The frequency of M0 was found in 84.6% and M+ was observed in 15.4%. 0.2% had stage 0, 4.3% had stage I, 28.8% had stage II A, 19.3% had stage II B, 31.6% had stage III, and 13.4% had stage IV. There were 6.3% patients had grade 1, 31.7% patients had grade 2, 28.7% patients had grade 3. There are 5% patients had T0, 5.2% had T1, 44.2% had T2, 13.2% had T3 and 30.1% had T4. Nodal status was positive in 42.6% patients and negative in 57.1%. Hormone receptor was positive in 42% and negatives in 58%.

The mean age at diagnosis in the Her2 positive was 47.94±11.75 and Her 2 negative was 50.55±12.84. Mean tumour size was found 2.93±1.57 and 2.72±1.55 in Her 2 positive and negative respectively. The mean difference of age ($p<0.001$) and tumour size ($p<0.001$) in Her 2 positive and negative was found highly significant. The mean age at diagnosis of luminal A was 55.16±12.53, luminal B was 51.09±12.56, Luminal B Her2 positive was 47.96±11.89, Her 2 was 47.92±11.64 and Triple negative was 46.73±12.15. The mean tumour size in luminal A, luminal B, B her, Her 2 and Triple negative was 2.64±1.39, 2.72±1.53, 2.90±1.54, 2.95±1.59 and 2.78±1.68 respectively. In luminal classification, there was also highly significant difference was found in mean age ($p<0.001$) and tumour size ($p<0.001$).

The association of Her 2 was significant with tumour Size (T size), metastasis, stage, grade, ki-67 and hormone receptor ($p<0.0001$) while the insignificant association was found with nodal status ($p=0.694$). T-size, metastasis, stage, grade, nodal status, ki-67 and hormone receptor were also highly associated with luminal classification ($p<0.0001$).

Binary logistic regression was applied to find an association between all the factors and Her2. The significant association of Her 2 was found with T0, T2, T3, metastasis, stage 0, stage II A, stage II B, stage III, grades (1, 2, 3), nodal status, hormone status, ki67 High which are associated significantly with Her 2. Luminal B is associated significantly with metastasis, grade and hormone receptor. Luminal B Her2 positive and Her2 were statistically associated with metastasis, grade and Ki67. The statistical significance of triple negative was also found with metastasis, grade and Ki67.

Discussion

It is well known that Breast cancer is heterogeneous disease especially in terms of biology, tumour behaviour and treatment response [7,8]. After the St. Galen guidelines that Immuno-histo-chemically tumour subtyping may be equated to Genetic assays, more utilization of these markers is seen especially in health care in under resource areas like ours [9]. Luminal B like (25.9%) and triple negatives (25.7%) were the commonest variety seen and overall Her2 positivity was seen in 30.1% of the patients. Luminal A-like disease with good prognosis is seen only is 18.3% of the cases which is in contrast to the figures from other areas reported to be 27.1% by Smriti Tiwari et al., 51.6% by Ahoua B Effect et al., Lin Ch 67% and it has been reported to be as high as 74.3% by Ahmed Abdel-Latif [10-14]. Luminal B like was the commonest type seen in our patients, like in Columbian women which were 37.2% [15]. Triple negative comprised of 25.7% of the cases, in some studiesit was reported to be much higher in African andas high as 82.2% [16-18].

In our patients, T2 was the commonest size (44.2%), grade 2 (31.7%) and Stage 2 (48%) was most frequently seen. This was the same reported by Ahmed Abdel-Latif and Kumar et al. [19]. The mean age at diagnosis was 49.76 in our study, which is much younger than western data. In luminal classification, a highly significant difference was found in mean age ($p<0.001$) and tumour size ($p<0.001$).

In our study 42.6% had a Node-positive disease, others have reported a higher rate of node-positive disease reaching as high as 75% from a local study, possible reason could be that our data is collected from a private tertiary care hospital [20]. Although there was a significant difference seen in various subtypes, this was not statistically significant when compared between Her2 positive and Her2 negative. The possible reason given is that in tumours with disseminated potential like triple negatives spread is through haematogenous route into systemic circulation rather than regional lymph nodes [21]. This could be one of the reasons that patients' with triple negative disease are considered to have an aggressive disease and poor survival in various reported studies [22-25].

In our study these patients with triple-negative disease were younger (Mean age 46.73) and had higher grade (Grade 3 in 67%), T1 was seen in only 10% of the cases, T2 was the commonest size (47%) and stage 2 was the commonest stage seen in around 50% of the cases, which is comparable to other studies by Onitilo and Parisewho had the similar results [26]. We also noted a high proliferate index (Ki67 high in 40%) in this group of patients.

Her positive disease is associated with aggressive disease and poor outcome [27]. In our study Her2 positive patients were seen to have younger age (mean 47 Years) as compare to luminal type where mean age in our study was 53 years. They were larger in size (T4 in 37%) at presentation as compare to Her2 negative, which was statistically significant. The commonest stage was stage 2 seen in 40% of patients and they had a high grade (Grade 3 was seen in 56%).

The significant association of Her 2 was found with T2, T3, and metastasis, stage II, stage III, grades (1, 2 and 3), nodal status, hormone status, High ki67. Though considered to have a bad outcome, when treated appropriately with chemo-therapy and anti-Her 2 medication, it may improve the course of the disease and outcome.

So, in breast cancer there is biological heterogeneity, leading to subgrouping on the basis of immune histo-chemistry to a fair extent. So each group has a specific profile which may improve the approach to therapy and leads towards personalized therapy of breast cancer.

Conclusion

IHC assignment into Luminal subtypes is clinically informative in our patients and routinely using this in our practice could identify patients that may need a more aggressive treatment to reduce the likelihood of recurrences.

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