

## Basal-Like Carcinomas of The Breast – An Intriguing Entity

Naila Kayani

Breast cancer is a diverse disease, encompassing many morphological and molecular genetic entities. It has also emerged as a heterogeneous disease, with respect to therapeutic response to treatment. Breast cancer is the commonest type of cancer in women both in developed world and developing countries. It is also the most common cancer in women, as reported from most regions of Pakistan.<sup>1</sup>

In Asia, Pakistan is amongst the countries with the highest incidence of breast cancer. Age standardized incidence rate per 100,000 population of breast cancer for Pakistan is 50.01 as compared to 19.1 for neighbouring India and 18.0 for China.

Invasive ductal carcinoma-No specific type (IDC-NST) is the most prevalent histological type and constitutes as many as 85% of malignant breast tumours.<sup>2,3</sup> Traditionally, histological grade was considered one of the best predictors of the tumour behaviour in invasive ductal carcinoma. The grade is based on histological parameters i.e. tubule formation, nuclear pleomorphism and mitotic activity. It is referred to as the modified Bloom and Richardson grading system and it places the tumours into three histological grades designated as I, II and III. The standard practice is to provide histological grade in all breast cancer reports at laboratories. While, grade I is associated with good to excellent and grade III has the worst prognosis. It must be kept in mind that other determinants such as tumour size and stage are of great significance too. In addition to morphology particular histological types also exist which denote their own prognostic significance such as papillary, mucinous, lobular, metaplastic, medullary etc.

The hormone receptor status i.e. estrogen receptor/progesterone receptor (ER/PR) assessment is now part of the prognostic work-up for carcinoma patients. More recently following successful clinical trials for Trastuzumab, HER2/neu has become a vital part of routine pathological work-up. However, it is observed that patients with histological similarities do show different clinical course and outcome.

It was proposed that the phenotypic diversity of breast tumours may be accompanied by a corresponding diversity in gene expression. Now, it has been demonstrated that this difference in clinical course of the

patients with histological similarities is due to differences at molecular level. DNA micro array profiling has shown distinct and reproducible subtypes of breast cancer associated with different outcomes. The gene profiling has shown five distinct subtypes of breast carcinomas: luminal A, luminal B, normal breast like, human epithelial growth factor receptor 2 over expression and basal-like.

The basic unit of breast is the terminal duct lobular unit and it has two distinct types of epithelium are formed in the human mammary gland i.e. basal (and/or myoepithelial-stained with cytokeratin 5/6) and luminal (stained with cytokeratins 8/18).

Thus, within the category of IDC-NST, grade III infiltrating ductal carcinomas (IDC) a subset exists which exhibits negativity for estrogen receptor/progesterone receptor (ER/PR) and HER2, so called triple negative. Heterogeneity has been found in this group and a proportion show a more aggressive pattern of disease. Gene expression studies using microarray have shown that within this group, named so because the neoplastic cells of this tumour constantly express genes usually found in normal basal/myoepithelial cells of the breast.

Basal-like breast carcinomas, as defined by gene expression microarray analysis, accounts for up to 15% of all breast cancers. This group is said to have a triple negative profile (ER-, PR-, HER2-). However, they are not identical to the so-called triple negative breast cancers, since the overlap between both terms is not complete. They are characterized by expression of basal cytokeratins (CK5/6, CK14), EGFR, etc.<sup>1,4,5</sup> The combination of ER and HER2 negativity and CK5/6 and EGFR positivity has 76% sensitivity and 100% specificity for identification of basal like breast cancers.<sup>6</sup> This group is said to have high histological grade, high mitotic indices, central zonal necrosis and prominent lymphocytic infiltrate. These are also reported to have a distinct pattern of spread, mostly hematogenous with lung and brain metastasis. This subset also includes medullary carcinomas and metaplastic breast carcinomas amongst others. Basal breast cancers share a similar protein expression pattern compared to physiological stem cells in the breast. The stem cells have the ability to differentiate into special types. Further investigation of basal tumours should enable penetrating insights into the relationship between breast cancer cells and their putative progenitor cells or cell of origin, respectively. Evidence is growing that physiological, organ-specific stem cells are the major target in the pathogenesis of different cancer entities, including breast cancer. The triple negative phenotype is

*Correspondence:* Dr. Naila Kayani, 67/11, 9th Street, off Khyaban-e-Badar, Defence Phase VI, Karachi.  
E-mail: [naila.kayani@aku.edu](mailto:naila.kayani@aku.edu)

Received June 09, 2010; accepted June 30, 2010.

increasingly used as a surrogate marker for basal-like breast cancer as it has the advantage that these stains are already used routinely in the prognostic clinical work-up of breast cancer patients. However, as stated earlier there is evidence that the group of triple negative cancers is heterogeneous and does not comprise a single entity and has an aggressive course.<sup>4-9</sup> The expression of basal cytokeratins (CK 5/6 and CK14) and more recently c-kit in this subset of grade III IDC-NST tumours is associated with a significant shorter disease free survival than those with triple negative cancers lacking the expression of basal markers. Immunohistochemical markers for this subset, a technique readily available in well equipped histopathology laboratories is being used as an alternative to DNA microarray, routine diagnostic work-up in the West.

Furthermore, it has been shown by studies that the differential staining of CK 14 can further categorize the basal alike subtype into the so called good and bad basal tumours of the breast.<sup>10</sup> Therefore, identification of these tumours with a potential of a more aggressive clinical behaviour is now possible through surrogate markers, making its identification a significant step in diagnosis. On the other hand understanding its biological progress is equally important in fully exploring the treatment options for patients.

#### REFERENCES

1. Bhurgri Y, Kayani N, Shaheen Y, Faridi N, Pervez S, Usman A, *et al.* Patho-epidemiology of breast cancer in Karachi '1995-1997'. *Asian Pac J Cancer Prev* 2007; **8**:215-20.
2. Banerjee S, Reis-Filho JS, Ashley S, Steele D, Ashworth A, Lakhani SR, *et al.* Basal-like breast carcinomas: clinical outcome and response to chemotherapy. *J Clin Pathol* 2006; **59**:729-35. Epub 2006 Mar 23. Comment in: *J Clin Pathol* 2007; **60**:958.
3. Jones C, Ford E, Gillett C, Ryder K, Merrett S, Reis-Filho JS, *et al.* Molecular cytogenetic identification of subgroup of grade III invasive ductal breast carcinomas with different clinical outcomes. *Clin Cancer Res* 2004; **10**:5988-97.
4. Sorlei T, Perou CM, Tibshirani R, Aas T, Geisler S, Johnsen H, *et al.* Gene expression patterns of breast carcinomas distinguish tumour subclasses with clinical implications. *Proc Natl Acad Sci USA* 2001; **98**:10869-74.
5. Sotiriou C, Neo SY, McShane LM, Korn EL, Long PM, Jazaeri A, *et al.* Breast cancer classification and prognosis based on gene expression profiles from a population-based study. *Proc Natl Acad Sci USA* 2003; **100**:10393-8. Epub 2003 Aug 13.
6. Nielsen TO, Hsu FD, Jensen K, Cheang M, Karaca G, Hu Z, *et al.* Immunohistochemical and clinical characterization of the basal-like subtype of invasive breast carcinoma. *Clin Cancer Res* 2004; **10**:5367-74.
7. Dent R, Trudeau M, Pritchard KI, Hanna WM, Kahn HK, Sawka CA, *et al.* Triple-negative breast cancer: clinical features and patterns of recurrence. *Clin Cancer Res* 2007; **13**:4429.
8. Tischkowitz M, Brunet J, Begin LR, Huntsman DG, Cheang MC, Akslen LA, *et al.* Use of immunohistochemical markers can refine prognosis in triple negative breast cancer. *BMC Cancer* 2007, **7**:134.
9. Reis-Filho JS, Tutt AN. Triple negative tumours: a critical review. *Histopathology* 2008; **52**:108-18.
10. Haupt B, Ro JY, Schwartz MR. Basal-like breast carcinoma: a phenotypically distinct entity. *Arch Pathol Lab Med* 2010; **134**:130-3.

