The Ethnic Profile of Triple-Negative Breast Cancer

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The article in this issue of ONKOLOGIE by Tian et al. [1] describing a series of triple negative breast cancers in a population of Chinese women joins the growing literature describing this sub-class of breast cancer within specific ethnic groupings. The immunohistochemical phenotype of oestrogen receptor (ER), progesterone receptor (PgR) and the HER-2 receptor negative breast cancer has been apparent for many years but its existence was highlighted by the expression RNA microarray work of Perou et al. and others that demonstrated a molecularly distinct group of breast cancers characterized by under expression of these three receptors, up-regulation of components of proliferation pathways and an expression profile that clustered with that of breast cancers arising in BRCA 1 mutation carriers [2, 3].

The triple negative subgroup overlaps with the morphologically distinct group of 'basal-like breast cancers', characterized by high mitotic count, central necrosis, frequent apoptotic cells, a stromal lymphocytic response and expression of myoepithelial markers (cytokeratins 5, 6, 14 and 17) [4, 5]. The triple negative subgroup of breast cancers is not homogeneous in terms of morphology, as it includes cancers with metaplastic, atypical or typical medullary and adenoid cystic appearance [4–7].

Clinically, triple negative cancers are characterized by high probability of systemic disease, and in particular development of lung and brain metastases [8, 9]. However, there is again heterogeneity as some subgroups, for example adenoid cystic carcinoma of the breast, are associated with an excellent prognosis [10]. Despite their aggressive natural history, triple negative breast cancers are more likely to achieve a complete pathological response to pre-operative chemotherapy (pCR) than other breast cancer types [11], and it appears that these patients with marked chemosensitivity have a relatively good chance of long-term survival [12]. Furthermore, although most studies demonstrate an association between the triple negative phenotype and poor outcome, some studies suggest that this negative association loses significance after 10 years, suggesting that patients that survive the first few years are no

more likely to relapse than other breast cancer sub-types [13, 14]. Thus, universal negativism about triple negative breast cancer may not be justified.

The profile of breast cancer in terms of age of onset and age distribution of molecular subgroups of the disease varies across the major ethnic subgroups, with Asian populations appearing demographically distinct. It is clear that incidence of breast cancer is much lower in Asian as compared to other ethnic groups. An analysis of data from the Surveillance, Epidemiology, and End Results (SEER) database and Osaka Cancer Registry (1978–97) showed overall age-adjusted incidence rates per 100,000 woman-years were highest in Whites (in SEER) (87.6), followed by Blacks (in SEER) (80.0) and lowest in Osaka (21.8). The Japanese population in this study was distinct in lacking the preponderance of postmenopausal breast cancer seen in both White and Black populations [15]. This preponderance of postmenopausal breast cancer in White and Black populations has been attributed to a complex interplay of life style factors [16] and access to healthcare, in particular breast screening [17]. It is not clear to what extent the demographics of Black Americans reflect those in other Black populations and indeed how representative the Japanese population is of other Asian ethnic subgroups.

Much has been written about the triple negative breast cancer in Western populations where it accounts for approximately 10–15% of all breast cancer cases [4, 18]. It has been consistently reported that the triple negative phenotype is proportionally more common in Black populations including women with Nigerian ancestry (58% in one study) [19] and within African populations in the US (20–21%) [18, 20], with a striking preponderance for pre-menopausal women. This demographic may be in part due to underlying host (germ-line) genetic factors, including inherited polymorphisms. However, a case-control study of African American and White women (the Carolina Breast Cancer Study) showed that basal cancer cases were associated with exposure of a set of 'basal breast cancer risk factors', namely multiple live births which did not

breast feed, younger age at first full-term pregnancy, use of medications to suppress lactation and elevated waist-hip ratio [21]. The authors suggest that 68% of basal-like breast cancer could be prevented by promotion of breast feeding and reduction of abdominal adiposity.

Relatively little has been written about this disease entity within Asian populations, and in particular Chinese populations. Within the small cohort of 116, presumably unselected, breast cancer patients described in this paper, the median age at diagnosis was 47 years and the triple negative immunophenotype accounted for 19% of cases with a median age of onset of 50 years. A Korean study of 776 female breast cancer cases reported a similar proportion (14.7%) of cancers to be basal-like, defined by immunopositivity for one or more basal markers and triple negativity, and a similar mean age of diagnosis (47.7 years) [22]. However, a Japanese study of 793 breast cancer cases reported only 7% of cancers to be triple negative, and the median age was slightly higher at 54 years [23]. It is also noteworthy that the triple negative phenotype in this population of Japanese women was associated with a 5-year overall survival of 86.2%, much higher than in many other series. Comparisons between studies must be undertaken with caution and while these discrepancies may be due to the small numbers concerned, differences in the intrinsic biology of breast cancer in different Asian populations or issues around access to healthcare cannot be excluded.

Very few conclusions can be drawn from this cohort of 22 cases of triple negative breast cancer, but, in keeping with other series, it suggests inferior outcome relative to other breast cancer types. As compared to 94 cases of 'non-triple negative cancer', and with a long median follow-up (96 months), 54.3% of the triple negative cases developed distant relapse compared to 21.2% ($p < 0.05$). This difference is striking but information relating to the clinicopathological features of the 'non triple negative group' is lacking.

To date, all the published data with regard to Asian women has been based on immunohistochemical phenotype and no molecular based studies exist. Such studies would be of interest in terms of examining whether there are any differences between the molecular signature of 'Western triple negative' as compared to an 'Asian triple negative' breast cancer, or indeed any differences between different Asian sub-populations.

One fifth of the world's women live in China. Whilst the incidence of breast cancer in most of China is currently low compared with the Western world, the incidence is rising rapidly in Shanghai [24] and Hong Kong [25] and set to rise elsewhere in the country as lifestyles change. Careful documentation of the changes in the incidence and composition of breast cancer in relation to lifestyle over the next few years may help our understanding of the biology of breast cancer and help China respond with an evolving epidemic.

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