Cirugía y Cirujanos. 2015; 83(1): 1-2

CIRUGÍA y CIRUJANOS

Órgano de difusión científica de la Academia Mexicana de Cirugía

Fundada en 1933

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EDITORIAL

Current concepts in breast cancer☆

Conceptos actuales en el cáncer mamario

Genome analysis as a whole has changed the understanding of cancer in general and has specifically contributed to the identification of molecular subtypes of breast cancer, each of which has specific genetic and clinical characteristics.

In 2000, Perou et al.[1] were the first to prove that the phenotypic diversity of breast cancer corresponds to its diversity in the expression patterns of genes, and identified molecular subtypes of breast cancer, known also as "intrinsic subtypes," including: luminal A, luminal B, HER2, triple negative and "with phenotype similar to breast" (of which the existence is controversial).

The assessment of breast carcinomas with immunohistochemistry markers to detect the expression of oestrogen receptors (ER), progesterone receptors (PR), the receptor of the human epidermal factor 2 (HER2) and Ki-67 act as subrogates that allow for the identification of the breast molecular subtypes.

Luminal A and B carcinomas express ER and PR, represent around 40-55% of breast carcinomas, tend to manifest in postmenopausal women, and they are generally of low degree. Breast carcinomas with HER2/neu overexpression represent 12 to 30% of all carcinomas. Their clinical course has significantly changed since 1998, with the introduction of trastuzumab. These tumours can be subdivided into those with or without the ER/PR expression[2].

Triple negative carcinomas represent 12 to 25% of cases and correspond to multiple subtypes, including those with a basal phenotype. These tumours show a greater histological degree and a greater index of cellular proliferation than the rest of the subtypes. They are more frequent in African American women (vs. non-African American, 26% vs. 16%, respectively), younger patients (vs. postmenopausal, 24% vs.15%, respectively), and in patients with BRCA1 mutations.

When compared with luminal A and B subtypes, triple negative carcinomas have a worse prognosis, mainly in the first 2 years after the initial diagnosis. Some studies have reported a lower tendency of these tumours to cause metastases in lymph nodes when compared to the carcinomas with HER2 overexpression (HER2)[2,3].

There is a lower percentage of local recurrences in the luminal groups vs. the triple negative carcinomas and the HER2. The administration of hormonal adjuvant therapy diminishes local recurrences in luminal A/B subtypes. 14.7% of local recurrences have been found in patients treated with placebo vs. 4.3% of the patients who received administration of tamoxifen for 5 years.

Recurrences occur earlier in triple negative carcinomas and HER2, and are produced later in luminals A/B.

Common sites for metastasis and correlation with molecular subtypes of breast cancer

Luminal A tumours with positive ER have the lowest risk of systemic relapse. The survival mean from the first metastasis is approximately 2.2 years, which is higher than any other subtype, including luminal B (1.6 years)[3].

HER2, without adjuvant treatment with trastuzumab, has a higher risk of recurrence than luminal A or B; the survival mean from the first metastasis is approximately 0.7 years.

Triple negative carcinomas have the highest risk of causing distant metastases in the long term, when compared to any other cancer subtype. The mean time of survival from the first metastasis in these patients is approximately 0.5 years. Unlike other subtypes, if a patient with triple negative carcinoma does not manifest metastasis in the first 7 years after the initial diagnosis, the chances of death due to breast cancer are significantly reduced[4].

Triple negative carcinomas usually tend to manifest distant metastases before a locoregional relapse takes place.

☆Please cite this article as: Alvarado-Cabrero I. Conceptos actuales en el cáncer mamario. Cirugía y Cirujanos. 2015; 83: 1-2.

Osseous metastases

The bone is the most common place for metastasis in almost all breast cancer subtypes (except for triple negative carcinomas); nearly 50% of these patients will develop events such as fractures, which may require radiotherapy as palliative treatment, or surgery.

Osseous metastases in patients with positive ER/PR can occur 10 to 20 years after the initial diagnosis[5].

Liver

Around 60-70% of women with breast carcinomas have hepatic metastases in the autopsy studies. The subtypes that express HER2 tend to metastasise more frequently in the liver.

Central nervous system

The metastases in the central nervous system appear with symptoms such as headaches, changes in mental status or nausea/vomiting. Metastases in the central nervous system are more common in younger patients and in those with triple negative carcinomas and HER2 treated with trastuzumab, with a lower risk for luminal A and B subtypes.

For patients with positive HER2 tumours, the metastases is deemed to occur after affecting visceral organs, which can be part of a stable disease or a disease that responds to therapy. Despite the fact that the trastuzumab prolongs average survival time, there is a higher proportion of metastases in the central nervous system in these patients[4,5].

Lung and pleura

Pulmonary metastases of breast cancer can appear as: solitary or multiple nodules, lymphangitic carcinomatosis and endobronchial metastases, and can copy pulmonary adenocarcinomas. Pulmonary metastases are less frequent in luminal A subtype.

The pleural disease due to breast cancer commonly appears with pleural effusion, which is generally unilateral and ipsolateral regarding the affected breast. The pleural condition is due to the secondary dissemination of cancer through the internal breast lymph nodes[5].

Conclusions

The great morphological and clinical heterogeneity of breast cancer has molecular bases. The functional assessment of the molecular pathways may become more relevant in the future, especially in the era of molecular targets.

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Received 21 October 2014; accepted 27 October 2014