CÁNCER DE MAMA

Oncoplastic surgery for the conservative treatment of breast cancer in Perú's National Cancer Institute.

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Ecancermedicalscience. 2018, 12.

Abstract

Background: Oncoplastic surgery for breast cancer (OPS) has been a surgical trend for the past 25 years. In 2012, OPS has been introduced as the standard treatment for a selected group of patients at the National Cancer Institute of Peru (INEN). The aim of this study is to describe our findings. Methods: This is a retrospective and descriptive study that identified demographics, tumour-pathologic features and includes patients solely treated since diagnosis until late follow-up at INEN. These OPS patients were identified from the conservative treatment patients group by review of medical charts and creation of a database for periods December 2005 through December 2015. Results: A total of 146 patients were ruled in by the inclusion criteria. All patients were Peruvian females, 56.2% being 51 or older. 93.8% had core biopsy diagnosis of breast cancer and 52.1% located at the upper outer quadrant. 79.5% patients had upfront OPS and the round block (43.2%) and reduction/mastopexy (23.3%) were the most used techniques. pT2 was the most frequent size (54.7%). We achieved negative margins in 134 patients (93.2%) in a single procedure. Of 29 patients, who had neoadjuvant treatment, 11 achieved pCR. Only 5.5% had pN2 or higher. 95.2% received complimentary external beam radiotherapy. Conclusions: OPS has proven to be a reliable surgical option, both for aesthetic and oncologic outcomes. Important points for achieving these results are breast surgeons having properly trained under the OPS philosophy and knowing the patients' characteristics for correct technique selection.

Células madre del cáncer: su participación en el cáncer mamario triple negative.

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Abstract

The breast cancer is the most common cancer diagnosed in women in the worldwide and it is considered as a public health problem. It is a heterogeneous disease with a high degree of diversity within the tumor, among tumors and also between in the patients. Within the subtypes of the breast cancer, the triple negative type is one of the most devastating cancers, with high rates of morbidity and mortality. Its current treatment is a challenge due to the loss of targets. The carcinogenesis that prevails today is based on the stochastic model, but recently, the cancer stem cell model is an alternative theory that proposed that there is a sub-population of the cancer cells capable of self-renewal and the multiline age differentiation which is responsible of the tumor regeneration, that could explain the heterogeneous lineages of the cancer cells and thus may play an important role in the initiation, the maintenance and the dissemination of cancer. In this work paper we review the most relevant current knowledge about the cancer stem cells in the triple negative breast cancer tumor subtype, focusing on the markers used to identify these cell populations and their use as a prognostic indicator of this disease, as well as their possible the participation in the carcinogenesis of this type of the breast cancer.

Genetics, tumor features and treatment response of breast cancer in Latinas.

Carlos A Castaneda, Miluska Castillo, Cynthia Villarreal-Garza, **Connie Rabanal, Jorge Dunstan, Gabriela Calderon, Miguel De La Cruz, Henry Guerra, Jose M Cotrina, Julio Abugattas & Henry L Gomez.**

Breast Cancer Management. 2018, Jan 24.

Abstract

Breast cancer is a heterogeneous and genetic disease that has variability according to ethnicity and race with respect to incidence, clinical characteristics and prognosis. The incidence of breast cancer is lower but mortality is higher in Latinas than Caucasians in the US series. Risk factors appear to have different prevalence and impact in Latinas. Breast cancer in Latinas has particular clinic-pathological features including younger age, higher rates of triple-negative subtype and advanced stages. Molecular studies find that Latinas from every region have a specific BRCA incidence and a recurrent mutation, as well as differences in activity of molecular pathways. Treatment response rates and toxicity have also been compared, and no difference was found between Latinas and other ethnic groups.

Pathological Response in a Triple-Negative Breast Cancer Cohort Treated with Neoadjuvant Carboplatin and Docetaxel According to Lehmann's Refined Classification.

Echavarria I, López-Tarruella S, Picornell A, García-Saenz JÁ, Jerez Y, Hoadley K, **Gómez HL**, Moreno F, Monte-Millan MD, Márquez-Rodas I, Alvarez E, Ramos-Medina R, Gayarre J, Massarrah T, Ocaña I, Cebollero M, Fuentes H, Barnadas A, Ballesteros AI, Bohn U, Perou CM, Martin M.

Clin Cancer Res. 2018 Jan 29.

Abstract

Purpose: Triple-negative breast cancer (TNBC) requires the iden- tification of reliable predictors of response to neoadjuvant chemotherapy (NACT). For this purpose, we aimed to evaluate the performance of the TNBCtype-4 classifier in a cohort of patients with TNBC treated with neoadjuvant carboplatin and docetaxel (TCb). Methods: Patients with TNBC were accrued in a nonrandomized trial of neoadjuvant carboplatin AUC 6 and docetaxel 75 mg/m2 for six cycles. Response was evaluated in terms of pathologic complete response (pCR, ypT0/is ypN0) and residual cancer burden by Symmans and colleagues. Lehmann's subtyping was performed using the TNBCtype online tool from RNAseq data, and germline sequencing of a panel of seven DNA damage repair genes was conducted. Results: Ninety-four out of the 121 patients enrolled in the trial had RNAseq available. The overall pCR rate was 44.7%. Lehmann subtype distribution was 34.0% BL1, 20.2% BL2, 23.4% M, 14.9% LAR, and 7.4% were classified as ER+. Response to NACT with TCb was significantly associated with Lehmann subtype (P = 0.027), even in multivariate analysis including tumor size and nodal involvement, with BL1 patients achieving the highest pCR rate (65.6%), followed by BL2 (47.4%), M (36.4%), and LAR (21.4%). BL1 was associated with a significant younger age at diagnosis and higher ki67 values. Among our 10 germline mutation carriers, 30% were BL1, 40% were BL2, and 30% were M. Conclusions: TNBCtype-4 is associated with significantly different pCR rates for the different subtypes, with BL1 and LAR displaying the best and worse responses to NACT, respectively.

Effect of CCL5 expression in the recruitment of immune cells in triple negative breast cancer.

Araujo JM, Gomez AC2, Aguilar A, Salgado R, Balko JM, Bravo L, Doimi F, Bretel D, **Morante Z**, Flores C1, **Gomez HL**, Pinto JA.

Sci Rep. 2018 Mar 20;8(1):4899.

Abstract

Triple negative breast cancer (TNBC) is the most aggressive form of breast cancer with limited options of targeted therapy. Recent findings suggest that the clinical course of TNBC may be modified by the presence of tumor-infiltrating lymphocytes (TILs) and chemokine's expression, such as CCL5. Diverse studies have shown that CCL5 suppresses anti-tumor immunity and it has been related to poor outcome in different types of cancer while in other studies, this gene has been related with a better outcome. We sought to determine the association of CCL5 with the recruitment of TILs and other immune cells. With this aim we evaluated a retrospective cohort of 72 TNBC patients as well as publicly available datasets. TILs were correlated with residual tumor size after neoadjuvant chemotherapy (NAC) and CCL5 expression. In univariate analysis, TILs and CCL5 were both associated to the distant recurrence free survival; however, in a multivariate analysis, TILs was the only significant marker (HR = 0.336; 95%IC: 0.150-0.753; P = 0.008). CIBERSORT analysis suggested that a high CCL5 expression was associated with recruitment of CD8 T cells, CD4 activated T cells, NK activated cells and macrophages M1. The CD8A gene (encoding for CD8) was associated with an improved outcome in several public breast cancer datasets.

Expressed Gene Fusions as Frequent Drivers of Poor Outcomes in Hormone Receptor-Positive Breast Cancer.

Matissek KJ, Onozato ML, Sun S, Zheng Z, Schultz A, Lee J, Patel K, Jerevall PL, Saladi SV, Macleay A, Tavallai M, Badovinac-Crnjevic T, Barrios C, Beşe N, Chan A, Chavarri-Guerra Y, Debiasi M, Demirdögen E, Egeli Ü, Gökgöz S, **Gomez H**, Liedke P, Tasdelen I, Tolunay S, Werutsky G, St Louis J, Horick N, Finkelstein DM, Le LP, Bardia A, Goss PE, Sgroi DC, Iafrate AJ, Ellisen LW.

Cancer Discov. 2018 Mar;8(3):336-353.

Abstract

We sought to uncover genetic drivers of hormone receptor-positive (HR+) breast cancer, using a targeted next-generation sequencing approach for detecting expressed gene rearrangements without prior knowledge of the fusion partners. We identified intergenic fusions involving driver genes, including PIK3CA, AKT3, RAF1, and ESR1, in 14% (24/173) of unselected patients with advanced HR+ breast cancer. FISH confirmed the corresponding chromosomal rearrangements in both primary and metastatic tumors. Expression of novel kinase fusions in nontransformed cells deregulates phosphoprotein signaling, cell proliferation, and survival in three-dimensional culture, whereas expression in HR+ breast cancer models modulates estrogen-dependent growth and confers hormonal therapy resistance in vitro and in vivo Strikingly, shorter overall survival was observed in patients with rearrangement-positive versus rearrangement-negative tumors. Correspondingly, fusions were uncommon (<5%) among 300 patients presenting with primary HR+ breast cancer. Collectively, our findings identify expressed gene fusions as frequent and potentially actionable drivers in HR+ breast cancer.Significance: By using a powerful clinical molecular diagnostic assay, we identified expressed intergenic fusions as frequent contributors to treatment resistance and poor survival in advanced HR+ breast cancer. The prevalence and biological and prognostic significance of these alterations suggests that their detection may alter clinical management and bring to light new therapeutic opportunities.

Clinicopathological predictors of long-term benefit in breast cancer treated with neoadjuvant chemotherapy.

Galvez M, Castaneda CA, Sanchez J, Castillo M, Rebaza LP, Calderon G, Cruz M, Cotrina JM, Abugattas J, Dunstan J, Guerra H, Mejia O, Gomez HL.

World J Clin Oncol. 2018 Apr 10;9(2):33-41.

Abstract

AIM: To investigate the survival impact of clinicopathological factors, including pathological complete response (pCR) and tumor-infiltrating lymphocytes (sTIL) levels according to subtypes, in breast cancer (BC) patients who received neo-adjuvant chemotherapy (NAC). METHODS: We evaluated 435 BC patients who presented and received NAC at the Instituto Nacional de Enfermedades Neoplasicas from 2003 to 2014. sTIL was analyzed as the proportion of tumor stroma occupied by lymphocytes, and was prospectively evaluated on hematoxylin and eosin-stained sections of the preNAC core biopsy. pCR was considered in the absence of infiltrating cancer cells in primary tumor and axillary lymph nodes. Analysis of statistical association between clinical pathological features, sTIL, pCR and survival were carried out using SPSSvs19. RESULTS: Median age was 49 years (range 24-84 years) and the most frequent clinical stage was IIIB (58.3%). Luminal A, Luminal B, HER2-enriched and (triple-negative) TN phenotype was found in 24.6%, 37.9%, 17.7% and 19.8%, respectively. pCR was observed in 11% and median percentage of sTIL was 40% (2%-95%) in the whole population. pCR was associated to Ct1-2 ($P = 0.045$) and to high sTIL ($P = 0.029$) in the whole population. There was a slight trend towards significance for sTIL ($P = 0.054$) in Luminal A. sTIL was associated with grade III ($P < 0.001$), no-Luminal A subtype ($P < 0.001$), RE-negative ($P < 0.001$), PgR-negative ($P < 0.001$), HER2-positive ($P = 0.002$) and pCR ($P = 0.029$) in the whole population. Longer disease-free survival was associated with grade I-II ($P = 0.006$), cN0 ($P < 0.001$), clinical stage II ($P = 0.004$), ER-positive ($P < 0.001$), PgR-positive ($P < 0.001$), luminal A ($P < 0.001$) and pCR ($P = 0.002$). Longer disease-free survival was associated with grade I-II in Luminal A ($P < 0.001$), N0-1 in Luminal A ($P = 0.045$) and TNBC ($P = 0.01$), clinical stage II in Luminal A ($P = 0.003$) and TNBC ($P = 0.038$), and pCR in TNBC ($P < 0.001$). Longer overall survival was associated with grade I-II ($P < 0.001$), ER-positive ($P < 0.001$), PgR-positive ($P < 0.001$), Luminal A ($P < 0.001$), cN0 ($P = 0.002$) and pCR ($P = 0.002$) in the whole population. Overall survival was associated with clinical stage II ($P = 0.017$) in Luminal A, older age ($P = 0.042$) in Luminal B, and pCR in TNBC ($P = 0.005$). CONCLUSION: Predictive and prognostic values of clinicopathological features, like pCR and sTIL, differ depending on the evaluated molecular subtype.

Células madre del cáncer: su participación en el cáncer mamario triple negativo.

Javier E. Enciso, **Carlos Castañeda,** Nathaly Enciso, Carlos E. Cisneros, Alejandro Fukusaki, Luis J. Alfaro, Nancy Rojas, **Carolina Belmar-López.**

Rev Venez Oncol 2018; 30(1):61-72.

Abstract

El cáncer de mama es el más comúnmente diagnosticado en mujeres en el mundo y se considera un problema de salud pública. Es una enfermedad heterogénea con alto grado de diversidad dentro del tumor, entre tumores y entre pacientes. Dentro de los subtipos del cáncer de mama se identifica el triple negativo, que es el más devastador, con altas tasas de morbilidad y mortalidad, su tratamiento actual es un desafío debido a la pérdida de receptores blanco. La carcinogénesis que predomina en la actualidad se basa en el modelo estocástico, pero recientemente, el modelo de células madre del cáncer ha propuesto una teoría alternativa que además trata de explicar la recidiva después de quimioterapia primaria, y plantea que hay una sub-población de células del cáncer responsable de la regeneración del tumor, que tienen capacidad de auto-renovación, diferenciación multilinaje, generando linajes heterogéneos de células cancerosas que pueden jugar un papel importante en la iniciación, mantenimiento y diseminación del cáncer. Se revisan conocimientos actuales más relevantes sobre células madre del cáncer en el subtipo tumor mamario triple negativo, al haber limitadas publicaciones en este tema, incidiendo en los marcadores que se utilizan para identificar estas poblaciones celulares y su uso como indicadores pronóstico de esta enfermedad, así como su posible participación en la carcinogénesis de este tipo de cáncer mamario.