Secretory Carcinoma of the Breast: Molecular Characterization of 12 Cases by Standardized Quantitative RT-PCR Analysis


Background: Secretory carcinoma (SC) is a rare subtype of invasive ductal carcinoma with fewer than 200 cases reported to date. SC was originally called “juvenile” carcinoma, as many cases occur in females and in males <50 years old. Most SCs are ER, PR, and HER2-negative (“triple negative”), but some express low levels of ER as detected by immunohistochemistry (IHC). Despite this biomarker profile, SC is known to have an indolent clinical course; most patients are cured with surgery, and the few patients who develop metastasis rarely die of their cancer. To help shed light on this paradoxical clinical behavior, we compared quantitative gene expression data for IHC-ER-positive SCs (N = 12) to ER-positive invasive ductal carcinoma, NOS (IDC-NOS; N = 427). We used the 21-gene Recurrence Score® (RS) testing.

Design: We evaluated 12 invasive carcinomas with classic morphologic features of the SC subtype that were IHC-ER-positive at the submitting site (2009-2015). Gene expression is quantitated on a scale from 2 to 15 (relative to reference genes), where each one-unit increment is associated with an approximate two-fold change in expression.

Results: SC patients (11 female, 1 male) ranged from 26 to 79 yrs (mean 52 yrs), similar to the age range of IDC-NOS (mean 58 yrs). There were distinct differences in gene expression. Mean ER expression was 6.5 (range 5.3 to 8.2), lower than that seen in IDC-NOS (mean 10.0, range 2.4 to 15.5). Mean PR expression was 4.1 (range 2.9 to 6.4), lower than that seen in IDC-NOS (mean 7.3, range 2.0 to 13.7). Compared to IDC-NOS, mean expression of the proliferation genes (Ki-67, STK15, SURV, CCNB1, MYBL2) was 1 unit lower, mean expression of the ER gene group (BCL2, CEGBP1, ER and PR) was 2.8 units lower, and mean expression of the invasion genes (STMV3 and CTSL2) was 1 unit higher in SC. Mean HER2 expression was lower in secretory carcinoma (8.7) than in IDC-NOS (9.2). No differences were seen in other assay genes (CD68, GSTM1, BAG1, and GRB7).

Conclusions: SCs have a distinct gene expression profile when compared to IDC-NOS. Some SCs express ER at low levels, detectable by both IHC and qPCR. Results of prognostic/predictive assays must be interpreted in the entire clinical and pathologic context. Per SOP, RS results are not reported for SCs.