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Human epidermal growth factor receptor-type 2 expression heterogeneity pattern in invasive breast carcinomas: frequency, distribution and relation to morphological variables

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Objective: To evaluate the spectrum of human epidermal growth factor receptor-type 2 (HER2) expression in primary invasive breast carcinomas, considering its heterogeneity and its relationship with morphological variables. **Methods:** This retrospective study analyzed HER2 expression and heterogeneity in invasive breast carcinoma cases from the São Paulo Federal University Hospital, between 2019 and 2023. Three observers evaluated the HER2 slides following the ASCO-CAP 2018 guidelines. Pathological variables were collected, and statistical analyses were performed using the IBM Statistical Package for Social Sciences (SPSS), version 26.0. **Results:** This study included 353 cases, with 29.5% under 50 years and 70.5% over 50. Left-sided tumors accounted for 54.1%. Invasive carcinoma of no special type was most common (91.8%), followed by invasive lobular carcinoma (7.4%). HER2 was negative in 83.9% and positive in 11.9%, with 4.2% classified as HER2 2+. Homogeneous HER2 expression was found in 81.3% of cases, mainly 0+ (80.8%), while 18.7% showed heterogeneity, primarily scattered (59.1%) or clustered (37.9%). Invasive lobular carcinoma cases were mostly homogeneous (92.3%). HER2 heterogeneity was significantly associated with histologic grade ($p=0.005$) and marginally with estrogen/progesterone expression ($p=0.060$), but not with tumor size ($p=0.071$). **Conclusion:** Heterogeneity was prevalent in HER2 expression, especially in invasive breast carcinoma, and should be addressed in pathology reports, especially in the antibody-drug conjugate scenario.

Keywords: breast neoplasms; ErbB-2 receptor.