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Area tematica

Breast cancer

Titolo

Predictors of HER2 gene amplification in immunohistochemistry score 2+ Early Breast Cancer according to 2018 ASCO/CAP guidelines: a single institution analysis.

Testo

Background
HER2 overexpression occurs in approximately 15-20% of invasive breast cancers (BC). From a pathological point of view HER2 positivity is defined by intense circumferential membrane complete staining in more than 10% of tumour cells in immunohistochemistry (IHC score 3+). When complete circumferential staining is weak to moderate (IHC score 2+) double probe in situ ibridation (ISH) is mandatory to define HER2 status. In 2018 ASCO/CAP guidelines were updated to provide additional guidance in HER2 equivocal cases to allow a greater discrimination between positive and negative cases. Our aim is to find predictors of HER2 positivity among IHC score 2+ early breast cancer specimens analysed according to 2018 ASCO/CAP guidelines.

Patients and Methods
253 cases of early BC diagnosed at Modena Cancer Center between November 2013 and August 2017 were identified. Stage, ISH result, hormonal receptor status (HR), proliferation index (MIB1), and histological grade were captured; menopausal status was available too. All IHC score 2+ cases were reclassified according to 2018 ASCO/CAP guidelines. The association between pathological tumour features, clinical characteristics and ISH positivity was assessed using Fisher test.

Results
Overall, 25.7% IHC score 2+ BC resulted HER2 amplified in double probe ISH. High tumour grade (G3 vs G1-2) and MIB1 > 20% significantly predict HER2 ISH amplification (p=0,0001). No correlation was found according to HR, stage, or menopausal status.
The majority (185; 98.4%) of HER2-ve BC were reclassified as group 5 (HER2/CEP17 ratio <2 and HER2 copy number <4 signals/cell) except for 3 specimens classified as group 4 (HER2/CEP17 RATIO <2 and HER2 copy number ³4 but <6 signals/cell). In HER2+ve group the majority (62; 95.3%) specimens were group 1 (HER2/CEP17 RATIO >2 and HER2 copy number =4 signals/cell), no specimen was group 2, and only 3 cases were classified as group 3 (HER2/CEP17 RATIO <2 and HER2 copy number >6 signals/cell).

Conclusion
In this IHC score 2+ BC series, reclassification according to 2018 ASCO/CAP guidelines identified only 4.6% group 3 and 1.6% group 4 cases. The routinely assessment of grading and proliferation index could help to predict HER2 amplification in IHC score 2+ samples even if it must not substitute ISH assay in determining eligibility for HER2 targeted therapies.

Parole Chiave

1. Breast Cancer
2. HER2
3. immunohistochemistry

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