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Metaplastic breast carcinomas exhibit EGFR, but not HER2, gene amplification and overexpression: immunohistochemical and chromogenic *in situ* hybridization analysis

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Abstract

Introduction Metaplastic breast carcinomas constitute a heterogeneous group of neoplasms, accounting for less than 1% of all invasive mammary carcinomas. Approximately 70–80% of metaplastic breast carcinomas overexpress the epidermal growth factor receptor (EGFR). Human epidermal growth factor receptor (HER)2 and EGFR have attracted much attention in the medical literature over the past few years owing to the fact that humanized monoclonal antibodies against HER2 and therapies directed against the extracellular ligand-binding domain or the intracellular tyrosine kinase domain of EGFR have proven successful in treating certain types of human cancer. We investigated whether HER2 and EGFR overexpression was present and evaluated gene amplification in a series of metaplastic breast carcinomas.

Method Twenty-five metaplastic breast carcinomas were immunohistochemically analyzed using a monoclonal antibody (31G7) for EGFR and two antibodies for HER2 (Herceptest and CB11) and scored using the Herceptest scoring system. Gene amplification was evaluated by chromogenic *in situ* hybridization using Zymed Spot-Light EGFR and HER2 amplification probe. The results were evaluated by bright field microscopy under 40× and 63× objective lenses.

Results Nineteen (76%) metaplastic breast carcinomas exhibited EGFR ovexpression, and among these EGFR amplification (defined either by large gene clusters or >5 signals/nucleus in >50% of neoplastic cells) was detected in seven cases (37%): three carcinomas with squamous differentiation and four spindle cell carcinomas. One case exhibited HER2 overexpression of grade 2+ (>10% of cells with weak to moderate complete membrane staining), but HER2 gene amplification was not detected.

Conclusion Metaplastic breast carcinomas frequently overexpressed EGFR, which was associated with EGFR gene amplification in one-third of cases. Our findings suggest that some patients with metaplastic breast carcinomas might benefit from novel therapies targeting EGFR. Because most metaplastic breast carcinomas overexpress EGFR without gene amplification, further studies to evaluate EGFR activating mutations are warranted.

CISH = chromogenic *in situ* hybridization; DFS = disease-free survival; EGFR = epidermal growth factor receptor; HER = human epidermal growth factor receptor; MBC = metaplastic breast carcinoma; OS = overall survival.