Expression of E-cadherin and c-erbB-2/HER-2/neu Oncoprotein in High-Grade Breast Cancer

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Summary

E-cadherin (E-CD) is an epithelial-specific cell adhesion molecule, whose expression is lost in invasive lobular (ILC) but not in invasive ductal carcinoma (IDC) of the breast. This cell adhesion system can be disrupted by tyrosine kinase c-erbB-2/HER-2/neu. We examined 106 cases of high-grade invasive breast cancer, including 91 IDCs, 12 ILCs and 3 pleomorphic lobular carcinomas (PLCs). We determined Nottingham histological grade and performed immunohistochemistry for estrogen and progesterone receptors (ER/PR), Ki-67, E-CD and c-erbB-2/HER-2/neu with subsequent fluorescence in situ hybridization. Amplification of c-erbB-2/HER-2/neu gene was observed in 55/91 (60.4%) of IDCs, 3/12 (25%) of ILCs and 1/3 (33.3%) of PLCs, and associated with positive axillary lymph nodes. E-CD expression was lost in 14/91 (15.4%) of IDCs, 10/12 (83.3%) of ILCs and 2/3 (66.7%) of PLCs. The loss of E-CD immunoreactivity in IDCs appeared to be associated with c-erbB-2/HER-2/neu gene amplification, negative ER/PR status and positive lymph nodes, whereas E-CD-positive ILCs tended to be HER-2/neu-positive. The biological significance of E-CD expression seems to be different in high-grade IDC and ILC. Oncogenic pathway mediated by c-erbB-2/HER-2/neu may affect the E-CD expression in most invasive ductal breast carcinomas in vivo.

Key words: ductal breast carcinoma - lobular breast carcinoma - E-cadherin - c-erbB-2/HER-2/neu - immunohistochemistry

Souhrn

Exprese E-cadherinu a c-erbB-2/HER-2/neu onkoproteinu v málo diferencovaných karcinomech prsu

E-cadherin (E-CD) je pro epitel specifická adhezní molekula, jejíž exprese se, na rozdíl od invazivních duktálních karcinomů, snižuje nebo zcela ztrácí u invazivních lobulárních karcinomů. O tyrozin kináze c-erbB-2/HER-2/neu je známo, že může expresi adhezního systému, jehož součástí je E-CD, narušit. Vyšetřili jsme 106 případů málo diferencovaných (G2-G3) invazivních karcinomů prsu, z toho 91 IDC, 12 ILC a 3 pleomorfní lobulární karcinomy (PLC). Provedli jsme imunohistochemické barvení estrogenového a progesteronového receptoru (ER/PR), Ki-67, E-CD a c-erbB-2/HER-2/neu a vyšetřili amplifikaci genu pro c-erbB-2/HER-2/neu pomocí fluorescenční in situ hybridizace. Amplifikace genu pro c-erbB-2/HER-2/neu byla pozorována u 55/91 (60,4 %) IDC, 3/12 (25 %) ILC a 1/3 (33,3 %) PLC a byla asociována s pozitivitou axilárních lymfatických uzlin. Ke ztrátě exprese E-CD došlo u 14/91 (15,4%) IDC, 10/12 (83,3 %) ILC a 2/3 (66,7 %) PLC. Ztráta imunoreaktivity E-CD v IDC byla asociována s amplifikací genu pro c-erbB-2/HER-2/neu, negativitou ER/PR a pozitivními lymfatickými uzlinami, zatímco ILC s pozitivním E-CD byly obvykle HER-2/neu pozitivní. Exprese E-CD má pravděpodobné odlišný biologický význam v málo diferencovaných IDC a ILC. Signální dráha c-erbB-2/HER-2/neu může ovlivnit expresi E-CD ve většině invazivních duktálních karcinomech prsu in vivo.

Klíčová slova: duktální karcinom prsu – lobulární karcinom prsu – E-cadherin - c-erbB-2/HER-2/neu - imunohistochemie

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E-cadherin (E-CD) is a calcium-dependent, epithelial-specific cell-cell adhesion molecule, whose reduced or lost expression is associated with tumor dedifferentiation and increased metastatic potential in human carcinomas (8). Many investigations suggest that E-CD protein expression is lost in invasive lobular (ILC) but not in invasive ductal carcinomas (IDC) of the breast (10, 16, 25, 29). It has been shown that loss of E-CD expression is an early event in the formation of ILC. The absence of E-CD induces a partial loss of epithelial differentiation and may account for the extended spread of lobular carcinoma *in situ* (LCIS) and the peculiar diffuse