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Is E-cadherin/catenin axis important in grade III ductal carcinomas?

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Keywords

Catenins, E-cadherin, grade III ductal carcinomas, immunohistochemistry

Context

Cadherins are glycoproteins, mainly expressed in epithelial cells, that mediate cell-cell adhesion and interact with the interior of the cell via intracellular proteins called catenins. Through interaction with α -actin, α -catenin influences cell motility. β - and γ -catenins compete with each other for cadherin-binding sites, and the genes encoding them have been proposed as an oncogene and a tumour suppressor gene respectively. Not much is known regarding E-cadherin and catenin expression in breast cancer. Although some studies have linked reduced E-cadherin expression with poor outcome, others have revealed no independent prognostic value. Recent research has found that retained membrane E-cadherin expression was surprisingly associated with shorter survival in a study employing grade I ductal tumours (see Additional information). This study investigated E-cadherin and α -, β - and γ -catenin protein levels in a cohort of 470 patients diagnosed with grade III ductal carcinomas.

Significant findings

E-cadherin was detected through membrane staining in 294 cases (62%) and in cytoplasmic staining in 169 cases (36%). Membrane expression of α -catenin was present in 419 cases (91%), while 382 cases (83%) showed cytoplasmic staining. Membrane expression of β - and γ -catenin was found in 362 cases (78%) and in 354 cases (77%) respectively, while cytoplasmic expression was detected in 284 cases (61%) and in 314 cases (68%) respectively. A notable association between membrane expression of E-cadherin and all the catenins was found, while presence of all the catenins shows an association with each other. Strong membrane and cytoplasmic E-cadherin and α -catenin expression was associated with positive oestrogen receptor (ER) status. Interestingly, patients with strong membrane expression of E-cadherin, α - and β -catenin had significantly shorter relapse-free and overall survival rates.

Comments

Membrane expression of E-cadherin and α - and β -catenin in grade III ductal carcinomas was associated with aggressive disease. Loss of E-cadherin function - believed to contribute to increased proliferation, invasion and metastasis - is well documented in lobular breast cancers. However, loss of heterozygosity within 16q, where the E-cadherin gene lies, is infrequent in grade III ductal carcinomas, so it was quite surprising that membrane staining was absent in 38% of the examined carcinomas. As no dyscohesion was detected, it was suggested that P-cadherin might be responsible for cohesion in some of these tumours. Future studies should investigate the role of E-cadherin and catenin expression in other ductal grades and histological carcinoma types.

Methods

Semiquantitative immunohistochemistry

Additional information

Tan DS, Potts HW, Leong AC, Gillett CE, Skilton D, Harris WH, Liebmann RD, Hanby AM: **The biological and prognostic significance of cell polarity and E-cadherin in grade I infiltrating ductal carcinoma of the breast.** *J Pathol* 1999, **189**:20-27 ([PubMed abstract](#)).

References

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