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Introduction

ErbB receptors are trans-membrane glycoproteins with tyrosine kinase activity. Especially in cancer, they are implicated in cell proliferation, transformation, angiogenesis, migration and invasion. The expression of ErbB receptors, has not been studied well in patients with CIN 3 and cervical cancer.

The main aim of our study was to investigate the role of ErbB receptors status among young patients with CIN 3 and cervical cancer.

Material and Methods

We evaluated retrospectively tissue specimens from 75 patients with CIN 3 and cervical cancer, that have been treated in the Division of Gynaecological Oncology of the University of Patras.

For ErbB receptors immunostaining, we used: anti-EGFR polyclonal antibody sc-03 (Santa Cruz Biotechnology Inc., Santa Cruz, CA, USA) in a dilution 1:20, anti-ErbB-2 monoclonal antibody CB11 (BioGenex Laboratories Inc., San Ramon, CA, USA) in a dilution 1:100, anti-ErbB-3 polyclonal antibody sc-285 (Santa Cruz Biotechnology Inc., Santa Cruz, CA, USA) in a dilution 1:100 and anti-ErbB-4 polyclonal antibody sc-283 (Santa Cruz Biotechnology Inc., Santa Cruz, CA, USA) in a dilution 1:200.

Statistical analyses were performed using IBM SPSS statistical package v.24 (IBM Corp. Armonk, NY).

Results

For ErbB-2 receptor, 8 cases were positive (10.7%) and 67 cases were negative (89.3%). For ErbB-3 receptor, 24 cases were positive (32%) and 51 cases were negative (68%). For ErbB-4 receptor, 37 cases were positive (49.3%) and 38 cases were negative (50.7%).

Moreover, we found a statistically significant correlation between ErbB-2 expression and invasive cervical cancer.

Discussion

The EGF system is present in human organs and play important role in cell proliferation, differentiation and apoptosis during embryogenesis and postnatal development. It has four receptors (ErbB-1, ErbB-2, ErbB-3 and ErbB-4) and numerous ligands.

ErbB receptors are trans-membrane glycoproteins with an extracellular region containing two ligand-binding domains, a transmembrane domain and an intracellular domain with tyrosine kinase activity. They catalyze the transfer of the γ phosphate of ATP to hydroxyl groups of tyrosines in target proteins.

Dysregulation of the EGF system signaling network is implicated in various disorders. Loss of control of the cell functions mediated by the EGF system signaling network is a hallmark of oncogenesis. Several types of human cancers associated with dysregulation of the EGF system signaling network.

Especially in cancer, EGF system becomes hyperactivated with various mechanisms (ligand overproduction, receptor overproduction, constitutive receptor activation).

Overexpression and structural alterations of ErbB-1 are frequent in various cancers. They associated with higher grade, disease progression, poor survival and resistance to radiotherapy and chemotherapy.

Overexpression of ErbB-2 is frequent in various cancers. It is an indicator of a more aggressive clinical behavior.

Overexpression of ErbB-3 is frequent in various cancers. Although ErbB-3 overexpression related with ErbB-2 positivity and lymph node involvement, a definitive relationship with survival has not been established.

Overexpression of ErbB-4 is frequent in various cancers. It is related with favorable prognosis in breast and bladder cancer.

Conclusion

All these differences in ErbB receptors status among young patients with CIN 3 and cervical cancer could be possibly attributed to well-known alterations in the clinical behavior of both entities. In this perspective, future studies are needed in order to elucidate the clinical role of ErbB receptors status in patients with CIN 3 and cervical cancer.

References

1. Ravazoula P, Androutsopoulos G, Koumoundourou D, Michail G, Kourounis G. Immunohistochemical detection of HPV proteins and c-erbB receptors in cervical lesion specimens from young women. *Eur J Gynaecol Oncol* 2006;27(1):69-72.
2. Pinion SB, Kennedy JH, Miller RW, MacLean AB. Oncogene expression in cervical intraepithelial neoplasia and invasive cancer of cervix. *Lancet* 1991;337(8745):819-20.

