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High cyclooxygenase-2 expression in stage IB cervical cancer with lymph node metastasis or prametrial invasion.

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[Objective] The enzymes cyclooxygenase(COX)-1 & -2 are necessary for the synthesis of prostaglandins. COX-2 is usually absent in normal cells and is upregulated and expressed as a product of the "immediate early" gene during pathologic processes. In previous studies, overexpression of COX-2 supresses apoptosis and is directly related to tumor growth. We have attempted to determine a relationship between the tumor invasion & metastasis of uterine cervical cancer and COX & apoptosis by comparing the protein expression of apoptosis, COX-1 & -2 in tumor tissues. [Methods] The subjects were 18 FIGO stage IB uterine cervical cancer patients who underwent surgery at the Ajou University Hospital. There were 9 cases with lymph node or parametrial involvement. All tissues obtained from the cases were subject to immunohistochemical staining for COX-1, -2 and TUNEL method for apoptosis detection, and the following results were obtained. [Results] Tumor tissues confirmed by cytokeratin were separated into tumor surface, tumor stroma and invasion site portions, and in which increased apoptosis was observed in the tumor surface & tumor stroma, but not in the invasion sites. COX-2 expression was observed in all tumor tissues, which was especially strong in the tumor invasion site. Therefore, in cases of uterine cervical cancer where tumor invasion is taking place, COX-2 is expressed strongly whereas apoptosis was absent. It is concluded that COX-2 expression may downregulate cell apoptosis at the site of tumor invasion. When the cases were divided into two groups with regard to the presence or absence of lymph node or parametrial involvement, there was statistically significant (Mann-Whitney U test) COX-2 expression seen microscopically in the tumor stroma (p-value=0.028) and tumor invasion site (p-value=0.040) compared to the tumor surface (p-value=0.499). In other words, in surgically treated stage IB cervical cancer patients, COX-2 was significantly expressed when lymph node or parametrial involvement was present. [Conclusion] These results suggest that the high expression of COX-2 in stage IB cervical cancer patients may downregulate apoptosic processes and thus enhances tumor invasion and metastasis.

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Expression of Epidermal Growth FactorReceptor(EGFR) in Cervical Tissue and Serum of Patients with Cervical Neoplasia

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Objectives: Epidermal growth factor receptor (EGFR) is overexpressed in the tissue of various malignancies including carcinoma of the breast, lung, esophagus, cervix, and ovary. In patients with cervical neoplasia, there may be a relationship between the expression of EGFR in cervical neoplastic tissue and serum obtained from the same patient.

Methods: The expression of EGFR was determined in cervical tissues from 23 cervical intraepithelial neoplasia(CIN) patients and 16 invasive cervical carcinoma patients using immunohistochemical staining and the level of serum EGFR extracellular domain was measured in serum from 17 CIN patients and 14 cervical carcinoma patients using enzyme-linked immunosorbent assay(ELISA).

Results: The expression of EGFR in cervical tissue was significantly increased as normal cervical tissue progressed to CIN then to invasive cervical carcinoma($p=0.009$). And the mean level of serum EGFR according to the histologic diagnosis of normal cervix, CIN, invasive cervical carcinoma was 23.18 ± 1.92 fmol/ml, 23.49 ± 8.95 fmol/ml, and 30.46 ± 19.72 fmol/ml, respectively. The mean level of serum EGFR was higher in invasive cervical carcinoma than that of normal cervix or CIN. But there was no significant statistical difference($p=0.471$). Also the mean level of serum EGFR according to the intensity of immunohistochemical staining in negative(-), weakly positive(+), positive(++), and strongly positive(+++) staining was 19.36 ± 3.12 fmol/ml, 20.99 ± 3.59 fmol/ml, 29.08 ± 16.86 fmol/ml, and 24.34 ± 10.35 fmol/ml, respectively. The mean level of serum EGFR in positive(++) and strongly positive(+++) staining was higher than in negative(-) staining, but there was no significant statistical difference($p=0.450$).

Conclusions: The authors believe that the expression of EGFR in cervical neoplastic tissue could be used as a marker for reflecting the malignant transformation of cervical epithelial cells. Although the mean level of serum EGFR in invasive cervical carcinoma was higher than in normal cervix and CIN, and the mean level of serum EGFR in positive(++) and strongly positive(+++) immunohistochemical staining was higher than in negative(-) staining, there was no significant statistical difference, possibly due to the limited number of cases in this preliminary study. So, the authors believe that the level of serum EGFR may have a similar role as a tumor marker like the EGFR expression in cervical neoplastic tissue. This study should be continued further with more cases and the relationship between the level of serum EGFR and prognostic parameters of uterine cervical carcinoma need to be analyzed.