Abstract

The role of the selected chemokine-receptor axis in the pathogenesis of endometrial cancer

Introduction

Molecular diagnostics in endometrial cancer (EC) include differentiation between four subtypes of the disease. Research on further molecular factors is still ongoing. Chemokines are a family of cytokines which play important role in inflammation in tumour microenvironment. They take part in the carcinogenesis by promoting i.e. proliferation, angiogenesis and epidermal-mesenchymal transition (EMT) through activation of multiple intracellular pathways. Their role in EC development remains unclear.

Methodology

97 patients were included in the research, of whom 49 were diagnosed with stage I-II EC and constituted a study group. Control group was formed by 48 patients who underwent hysterectomy due to non-oncological reasons. Clinical data was obtained from medical records. Tissue samples were collected during surgery and preserved in paraffin blocks. Nine genes encoding chemokines and their receptors were included to molecular analysis with a polymerase chain reaction (PCR) to compare their relative expression in EC and healthy tissue: CXCL12 (ligand)-CXCR4/CXCR7 (receptors), CCL2-CCR2, CCL20-CCR6, CXCL10-CXCR3. Genes which presented significant differences between study and control group were selected to further analysis with immunohistochemistry (IHC) to assess the expression of chemokines and receptors in the same groups of patients. These included CXCL12, CCL20 (higher expression in EC) and CXCL10 (lower expression in EC). IHC examination included both endometrial and stromal tissue and was evaluated using immunoreactive score (IRS). Clinical data, molecular features and IHC staining evaluation was then analysed with parametrical and non-parametrical tests followed by correlation analysis.

Results

36 patients were included to a molecular analysis which revealed significantly increased expression of CXCL10 (p=0,01) and CCL20 (p=0,001) genes in the study group. Contrarily, expression of CXCL12 in the study group was significantly lower (p=0,01). IHC staining performed on the group of 77 samples confirmed the overexpression of CXCL10 protein in endometrial tissue (p=0,006) in the study group. In the control group, there was a higher expression of CXCL12 chemokine in endometrial stroma (p=0,008). Incoherent results of IHC

compared with PCR were reported considering CCL20 expression, which was lower in the study group in both endometrial (p=0,002) and stromal tissue (p=0,002).

Conclusions

There was an overexpression of CXCL10 detected in non-advanced EC in molecular and pathological assessment. This might be considered favourable prognostic factor, as according to literature, CXCL10 plays a role in an inhibition of malignant transformation in various neoplasms. Inconsistent results of expression of CCL20 gene in PCR and protein in IHC indicate a need of further research, preferably with inclusion of patients diagnosed with an advanced EC. This applies also to CXCL12 and other genes or proteins evaluated in the research.