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IMMUNOEXPRESSION OF MATRIX METALLOPROTEINASES MMP-1, MMP-2, MMP-9 AND MMP-14 IN EXTRAGENITAL ENDOMETRIOSIS AND EUTOPIC ENDOMETRIUM

Eugeniu Cazacu[1], Eremei Zota[1], Claudiu Margaritescu[2], Radu Niguleanu[1], Ruslan Pretula[1]

[1]Nicolae Testemitanu State University of Medicine and Pharmacy of the Republic of Moldova, Department of morphopathology

[2]University of Medicine and Pharmacy, Craiova, Romania, Department of Pathology

Introduction

Endometriosis is a comon, benign, inflamatory, pathology, represented by the ectopic location of functional endometrial glands and stroma outside the uterine cavity [1, 2].

Matrix metalloproteinase (MMP) represents a large family zinc-dependent endopeptidases, involved in the degradation of the extracellular matrix in the process of endometrial cell implantation and are classified by their substrate specificity [7, 8].

Matrix metalloproteinases (MMPs) are essential in orchestrating proper physiological functioning of the endometrium; hence, alteration of MMP activities is considered as a critical factor for the development of endometriosis. MMPs are involved in the cellular event of epithelial-mesenchymal transition [10, 22].

Purpose

The aim of this study was to evaluate the immunohistochemical expression of matrix-metalloproteinases MMP1, MMP2, MMP9 and MMP14 in surgical excision specimens, collected from women with extragenital endometriosis compared to their expression in the normal endometrium.

Material and methods

The patient group consist 42 women with endometriosis, age range of 21-63 years (median 40), diagnosed and surgically treated at Department of Surgery, Obstetrics and Gynecology from *Gherghe Paladi* Municipal Clinical Hospital, *Sfantul Arhanghel Mihail* Municipal Clinical Hospital, Chisinau, the Republic of Moldova and Emergency County Hospital, Craiova, Romania. Location included: the anterior abdominal wall after caesarean operation – 20, inguinal hernia – 7, umbilical hernia – 4, perineal region – 1, appendix – 4, colon – 5, and ileum – 1case.

Table 1

Antibodies used in immunohistochemical study

Antibody	Tipe	Clone	Producer	Catalog number	Dilution	Antigen retrieval	External positive control
MMP-1	Mouse monoclonal	6A5	Acris	AM06648SU-N	1:200	0.1 M Citrate, pH 6	Granulation tissue
MMP-2	Mouse monoclonal	OTI4A11	OriGene	TA806846	1:100	1mM EDTA in 10mM Tris buffer (pH8.5)	Granulation tissue
MMP-9	Mouse monoclonal	5G3	OriGene	AM06662SU-N	1:200	0.1 M Citrate, pH 6	Granulation tissue
MMP-14	Mouse monoclonal	113-5B7	OriGene	AF8410	1:100	0.1 M Citrate, pH6	Granulation tissue

Results

The classical histopatological examination of the general expression of MMP-1, MMP-2, MMP-9 and MMP-14 revealed a diverse variability. For MMP-2, MMP-9, MMP-14 markers, the reaction positivity was variable not only from one case to another but also within each case, the latter being characterized by the identification of different areas within endometriosis.

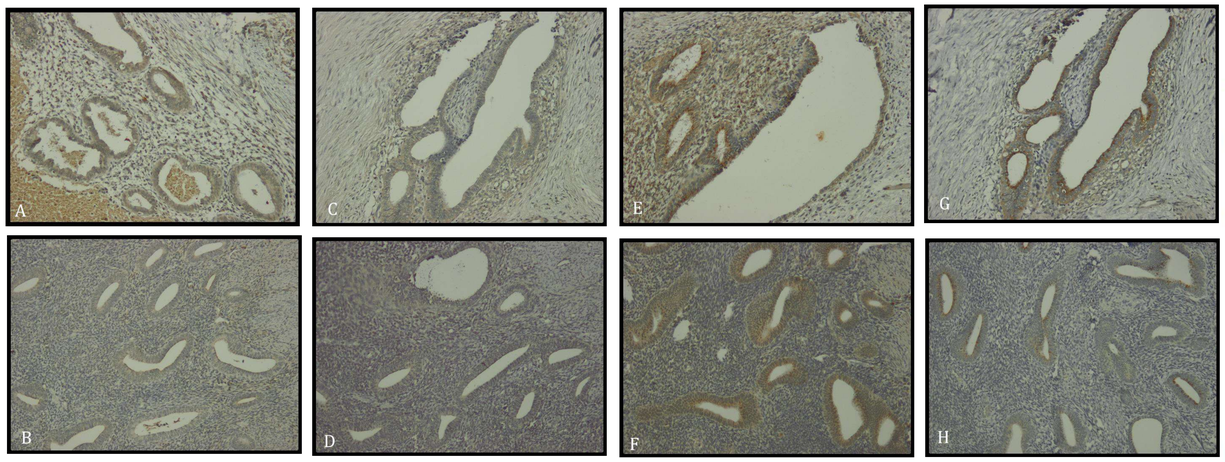

Fig. 1. Immunohistochemical reaction interpretation, A, C, E, G – endometriosis and B, D, F, H – normal endometrium.

Neagative reaction for MMP-1 in (A, B), moderate positive reaction for MMP-2 in (C, D), strong positive reaction for MMP-9 and MMP-14 in (E, F, G, H). IHC, obiective 10 × /0.30.

Immunohistochemical analysis has demonstrated the significant enhance of MMP-9 and MMP-14 expressions in endometriosis and in endometrium. The distinctive feature of MMP-9 and MMP-14 expression in endometriosis was considerable increase of its activity precisely on the border of endometriotic lesion and the peritoneum.

Conclusions

The MMP-9 and MMP-14 activity significant elevation, established on ectopic endometrium of women with endometriosis. Study of MMP-1, MMP-2, MMP-9 and MMP-14 activities in endometriotic lesions from women with endometriosis is perspective for further investigation in order to determine a possible role of matrix metalloproteinases in the development of invasiviness process in case of extragenital endometriosis.

Keywords

Endometriosis, matrix metaloproteinases, invasiveness potential.