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ABSTRACT

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MORPHOLOGICAL AND IMMUNOHISTOCHEMICAL CHANGES OF THE ENDOMETRIUM IN WOMEN WITH HYPERPROLIFERATIVE PATHOLOGY OF THE UTERUS AND REPRODUCTIVE DYSFUNCTION

Hyperproliferative pathology of the uterus (HPE) occupies one of the leading places in the structure of female infertility, leading to women's generative dysfunction in 80% of cases.

The aim of the study: to assess the immunohistochemical and morphological features of the endometrium in patients with hyperproliferative pathology of the endometrium and infertility.

Materials and methods. Forty endometrial samples from women with infertility and hyperproliferative pathology of the endometrium were examined: 20 samples of endometrium obtained from women with infertility and endometrial polyps (1 group) and 20 samples obtained from women with infertility and endometrial hyperplasia without atypia. The endometrium of 20 healthy women was examined as the control group.

Pipelle biopsy of the endometrium was performed in the luteal phase of the menstrual cycle in women of the main and control groups to obtain the material. The morphological and immunohistochemical features of the endometrium in women with infertility and hyperproliferative pathology of the endometrium were determined.

Histogram sections were stained with hematoxylin and eosin, and picrofuxin (Van Gizon's stain). An immunohistochemical study was performed with the polymer detection method of antigen application using the UltraVisionQuanto peroxidase polymer and DAB plus chromogen detection system to determine the expression of monoclonal antibodies to estrogen and progesterone receptors, natural killers CD-56 and CD-138.

The results of the investigation. Morphological examination of the endometrium of women with infertility and hyperproliferative pathology of the endometrium revealed a number of pathological changes: glandular and glandular-fibrous polyps of the endometrium (70–80%), atypical endometrial hyperplasia (10–20%), dyschronosis of endometrial receptivity (40–50%), morphological signs of chronic endometritis, positive expression of CD-138 (10%), as well as their combination.

Conclusions. Women with infertility and hyperproliferative pathology of the uterus and unsuccessful attempts at ART have expressed dyschronosis of receptivity of the endometrium on the background of reduced expression of endometrial natural killers and positive expression of CD-138. It is indicative of the dysregulation of immunological homeostasis on the local level, which may be the cause of disruption of blastocyst implantation processes, unsuccessful attempts of ART and lead to early pregnancy loss.

Key words: endometrial hyperplasia, endometrial polyps, uterine fibroids, ultrasound, hysteroresectoscopy.

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РЕЗЮМЕ

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МОРФОЛОГІЧНІ ТА ІМУНОГІСТОХІМІЧНІ ЗМІНИ ЕНДОМЕТРІЮ У ЖІНОК З ГІПЕРПРОЛІФЕРАТИВНОЮ ПАТОЛОГІЄЮ МАТКИ ТА ПОРУШЕННЯМ РЕПРОДУКТИВНОЇ ФУНКЦІЇ

Гіперпроліферативна патологія ендометрія (ГПЕ) займає одне з провідних місць у структурі жіночої безплідності, яка у 80 % випадків призводить до порушення генеративної функції жінок.

Мета дослідження: дослідити морфологічні та імуногістохімічні особливості ендометрія у пацієнок з гіперпроліферативною патологією ендометрія та безпліддям.

Матеріали та методи. Було досліджено 40 зразків ендометрію від жінок з безпліддям і гіперпроліферативною патологією ендометрія: 20 зразків ендометрія, отриманих від жінок з безпліддям і поліпами ендометрія (1 група) і 20 зразків, отриманих від жінок з безпліддям і гіперплазією ендометрію без атипії. Як контроль, був обстежений ендометрій 20 здорових жінок.

Для отримання матеріалу проводили Пайпель-біопсію ендометрію в лютеїнову фазу менструації циклу у жінок основної та контрольної групи. Визначали морфологічні та імуногістохімічні особливості ендометрію у жінок з безпліддям та гіперпроліферативною патологією ендометрію.

Зрізи гістограми фарбували гематоксиліном та еозином, а також пікрофуксином за ван Гізоном. Імуногістохімічне дослідження проводили за допомогою полімерного методу виявлення антигену виявлення за допомогою полімеру пероксидази UltraVisionQuanto і DAB плюс система виявлення хромогену для виявлення експресії моноклональні антитіла до рецепторів естрогену і прогестерону, натуральні кіллери CD-56 і CD-138.

Результати дослідження. Морфологічне дослідження ендометрію жінки при безплідді і гіперпроліферативній патології ендометрія виявило ряд патологічних змін: залозисті та залозисто-фіброзні поліпи ендометрію (70–80 %), атипова гіперплазія ендометрію (10–20 %), дисхроноз сприйнятливості ендометрію (40–50 %), морфологічні ознаки хронічного ендометриту, позитивна експресія CD-138 (10 %), а також їх комбінація

Висновки. У жінок з безпліддям і гіперпроліферативною патологією матки і невдалими спробами ДРТ є виражений дисх-

роноз сприйнятливості ендометрію на тлі зниження експресії природних кілерів ендометрію та позитивна експресія CD-138, що вказує на порушення регуляції імунологічного гомеостазу на місцевому рівні, який може бути причиною порушення процесів імплантації бластоцисти, невдалих спроб АРТ, ранньої втрати вагітності.

Ключові слова: гіперплазія ендометрія, поліпи ендометрія, міома матки, ультразвукова діагностика, гістерорезектоскопія.

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INTRODUCTION / ВСТУП

Hyperproliferative pathology of the endometrium in women of reproductive age is the cause of reduced reproductive potential, especially in women with unrealized reproductive plans. At present, the problem of atypical hyperplasia and endometrial polyps has become particularly important due to the increasing frequency of pathological processes in the structure of gynecological morbidity, which does not have a tendency to decrease and reaches up to 17.5% [1, 2].

There is no consensus on the causes of endometrial HPE: one group of researchers adheres to the inflammatory theory of their origin, other scientists associate it with hormonal disorders, including hyperestrogenemia, decreased progesterone, and some scientists believe that GPE is the result of changes in estrogen receptor expression – pathological increase in the local endometrial growth in response to circulating estrogens [3, 4, 5].

A number of studies have shown that chronic endometritis (CE) increases the risk of endometrial polyps 2.8 times and proves the role of inflammation in the development of this pathology, forming a clear indication for further management of the patient. It is established that the composition of subpopulations of endometrial leukocytes in chronic endometritis changes under the action of inflammatory agents, which corrects the tissue effects of hormones, the factors of growth and cytokines, affecting the expression of steroid hormone receptors in the endometrium [3, 4, 6, 7]. Processes associated with chronic inflammation indicate a key response of the uterus as a target

organ for the so-called pathological regeneration; that is, the inflammatory factor has an organic nature with damage to the structural elements of endometrial cells.

It is currently unknown which disorders and peculiarities of the interaction of hormonal and immune systems lead to increased proliferation of endometrial cells and the formation of endometrial polyps. In turn, it has been proven that chronic endometritis (or signs of stromal fibrosis) does not increase the likelihood of endometrial hyperplasia and proves the role of non-inflammatory genesis in its occurrence, confirming the leading pathogenetic role of hormonal homeostasis. Atypical endometrial hyperplasia is a systemic lesion with an impaired physiological cyclic expression of steroid receptors in the endometrium, which is functional in nature and depends on hormonal imbalance. The question of the relationship between the mechanisms that regulate proliferation processes and the morphofunctional and microbiological features of the endometrium remains open [8, 9, 10].

Objective: to study the immunohistochemical and morphological features of the endometrium in patients with hyperproliferative pathology of the endometrium and infertility.

Materials and Methods. The study was conducted on the clinical basis of the Department of Obstetrics, Gynecology and Family Planning Educational and Scientific Medical Institute of Sumy State University – Sumy Regional Clinical Perinatal Center during 2019–2021.

Forty endometrial samples from women with hyperproliferative pathology were studied: 20 samples of endometrium obtained from women

with infertility and endometrial polyps and 20 samples obtained from women with infertility and endometrial hyperplasia without atypia. The endometrium samples of 20 healthy women were examined as the control material.

Pipelle biopsy of the endometrium was performed in the luteal phase of the menstrual cycle in women with infertility and hyperproliferative pathology of the uterus and women in the control group. Exclusion criteria were women with severe somatic or mental pathology.

Hysteroscopy was performed on hard fiber optics company "KARLSTORZ" from the 7-th to the 11-th day of the menstrual cycle, after the removal of endometrial tissue, its histological examination was performed. The material was fixed in a buffered 10% formalin solution.

Pipelle biopsy was performed on days 18–23 of menstrual cycle using an aspiration probe. The aspiration probe was inserted into the uterine cavity to the bottom area and the contents were aspirated, resulting in the effect of "suction" to the walls of the uterine cavity and through the existing perforation material which enters the probe. The resulting material is placed in a vial with a 10% solution of neutral formalin. Histological examination of endometrium was performed according to the generally accepted method at the Department of Morphology of Sumy State University. The surgical material obtained by hysteroscopy and aspiration biopsy of the endometrium were subjected to morphological examination. The biopsy material was fixed in 10% neutral formalin. Further processing was performed according to the standard generally accepted unified method. Examination of histological preparations was performed on a Nikon Eclipse (Ci-E) light microscope using a digital video camera according to the recommendations of the software manufacturer.

The morphological and immunohistochemical features of the endometrium in women with infertility and HPE were determined. Histogram sections were stained with hematoxylin-eosin staining, and picrofuxin (Van Gizon). Pieces of endometrium were removed for electron microscopic examinations, fixed in 2.5% glutaraldehyde solution and postfixed with 1% osmium tetroxide solution on phosphate buffer. Further processing was performed according to the generally accepted method. Ultrathin sections made on an ultramicrotome UMPT-7 were contrasted with uranyl acetate, lead citrate according to the Reynolds

method and studied under an electron microscope PEM-125K. An immunohistochemical study was performed with the polymer detection method of antigen application using the UltraVisionQuanto peroxidase polymer and DAB plus chromogen detection system to determine the expression of monoclonal antibodies to estrogen and progesterone receptors, natural killers CD-56 and CD-138.

The obtained results were processed using standard statistical programs on an HP PREMIER EXPERIENCE personal computer with Microsoft Word 2010. Statistical processing was carried out using Statistics 10.

Results. In the analysis of retrospective data, the average age of patients with endometrial hyperplasia was 34.7 ± 3.9 (years), in the case of endometrial polyps – (29.8 ± 1.5) years, in combined endometrial pathology – (31.4 ± 2.9) years.

Morphological examination of the endometrium of women with infertility and hyperproliferative pathology of the endometrium revealed a number of pathological changes: glandular and glandular-fibrous polyps of the endometrium (70–80%), atypical endometrial hyperplasia (10–20%), dyschronosis of endometrial receptivity (40–50%), morphological signs of chronic endometritis, positive expression of CD-138 (10%), as well as their combination.

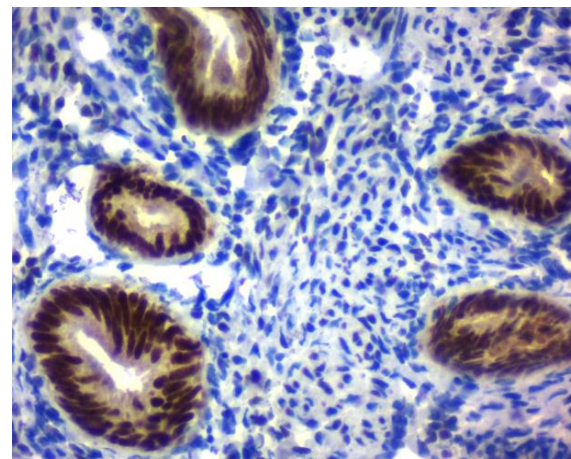


Figure 1 – Group 1. Increased expression of estrogen receptors in the nuclei of the epithelium of glands and stroma cells

Discussion. During the histological examination of endometrial samples from women of both groups, we found endometrial micropolyps in 90% of women in group 1 and in 70% of women in group 2. A combination of endometrial polyposis, morphological signs of luteal phase insufficiency, and dyschronosis of glandular changes was found in

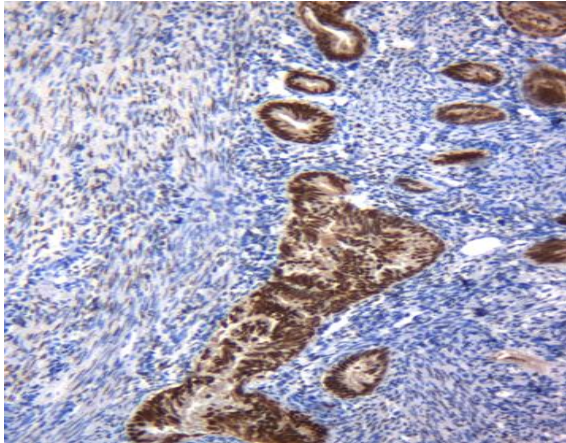


Figure 2 – Group 2. Increased expression of progesterone receptors in the nuclei of the epithelium of glands and stroma cells

30% of endometrial samples in group 1. Focal atypical endometrial glandular hyperplasia was found in 20% of women in group 2 and 10 % in group 1. There was a focal uneven increase in the expression of estrogens (up to 90–98%) and progesterone receptors (up to 60–70%) in the nuclei of glandular epithelium and stroma, especially in the group of women of group 1.

CONCLUSIONS / ВИСНОВКИ

Women with infertility and hyperproliferative pathology of the uterus and unsuccessful attempts at ART have a pronounced dyschronosis of receptivity of the endometrium on the background of reduced expression of endometrial natural killers, positive

PROSPECTS FOR FUTURE RESEARCH / ПЕРСПЕКТИВИ ПОДАЛЬШИХ ДОСЛІДЖЕНЬ

With regard to the women coming to a gynecologist with menstrual disorders, it is necessary to pay attention to the presence of HPE, and if women have chronic inflammatory diseases of the genitals organs, sanitation of these foci should be suggested in order to improve reproductive health. The risk

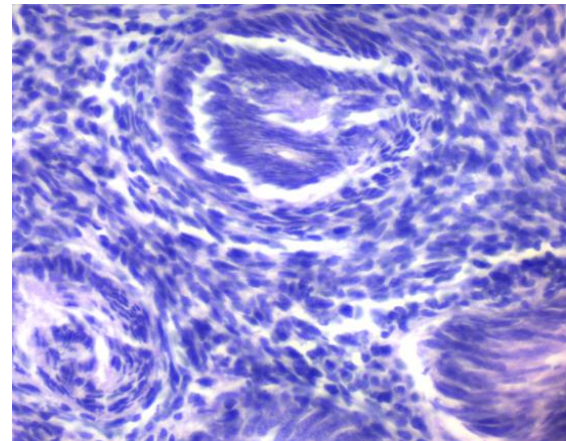


Figure 3 – Group 1. Micropolyp of glandular-stromal type. Hematoxylin-eosin staining

Expression of CD-56 showed a reduction in the endometrial stroma in 80% of group 1 and 40% of group 2, compared with the control group. Increased CD-56 expression in the endometrial stroma was observed in 30% of endometrial samples of group 2. Positive expression of CD-138 in endometrial was shown in 10% of samples of both study groups.

expression of CD-138 It is indicative of the dysregulation of immunological homeostasis at the local level, which may be the cause of disruption of blastocyst implantation processes, unsuccessful attempts of ART, and lead to early pregnancy loss.

assessment of gynecological diseases showed that the greatest attention should be paid to improving the diagnosis of endometriosis, as well as the prevention and treatment of oncological diseases of the female genital organs in order to prevent infertility.

CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

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