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EVALUATION OF THE PROLIFERATIVE ACTIVITY OF ENDOMETRIAL HYPERPLASIA IN THE POSTMENOPAUSAL PERIOD

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Abstract. The spectrum of the histological picture of the endometrium, as well as some markers of the proliferative activity of endometrial cell populations in postmenopausal patients with endometrial hyperplasia and uterine bleeding, were studied. The selection of therapy was carried out based on the somatic and genital status, the results of histological and immunohistochemical studies of the scraping of the uterine cavity. The effectiveness of therapy was assessed by the cessation of bleeding, normalization of hematological parameters, as well as by improving the general well-being of the woman.

Key words: Endometrial hyperplasia, endometrial histology, postmenopausal uterine bleeding, immunohistochemical markers - CD138, p53, Ki67, selection of therapy.

Proliferative processes in the endometrium (PPE): polyps, glandular and atypical hyperplasia in the structure of intrauterine pathology in pre- and postmenopausal patients occupy a leading position (60-70%) [2], tend to increase in the postmenopausal period [10], often recur (0 ,25-50%) [4] and may undergo malignancy. In turn, endometrial cancer is in first place in the structure of malignant gynecological diseases [9], in the structure of oncopathology it is located after breast, rectal and lung cancer , the highest incidence occurs in the age period of 60-64 years [11].

In the pathogenesis of hyperplastic processes of the endometrium, metabolic and endocrine disorders occupy a large place: changes in fat metabolism, metabolism of sex hormones in the pathology of the hepatobiliary system and gastrointestinal tract, immunity, thyroid function. In this regard, in patients with endometrial hyperplastic processes, obesity, hyperli pidemia, diabetes mellitus, hypertension, and metabolic syndrome are often noted [1,3].

The clinical significance of endometrial hyperplasia lies in its associated risk of progression to endometrioid endometrial cancer, and "atypical" forms of endometrial hyperplasia are considered precancerous lesions. The existing histological classifications of endometrial pathology are characterized by a wide and varying degree of diagnostic reproducibility, and, as a result, the management of patients remains extremely difficult. It should be noted that the WHO classification has a low level of reproducibility of diagnoses [5,9].

At the same time, the constant development of new technologies in medicine makes it possible to revise the known postulates of the diagnosis and treatment of various diseases. Considering the variety of data on the methods of examination and treatment of patients with hyperplastic processes in the endometrium, there is a clinical need to develop algorithms for managing patients according to age and pathological and morphological picture. Modern positions of pathogenetic features of endometrial hyperplastic processes. According to the generally accepted point of view, the leading role in the genesis of hyperplastic processes in the endometrium is assigned to the effects of elevated estrogen concentrations [6,12].

Currently, there is no doubt that hysteroscopy is the most informative instrumental diagnostic method for HPE. On examination, an unevenly thickened, folded endometrium

with a pronounced vascular pattern is visualized. The change in pressure in the uterine cavity when it is stretched by liquid media makes it possible to visualize the wave-like movements of the mucous membrane - a sign of "underwater plants". A distinctive feature of the cystic form of glandular hyperplasia is the presence of multiple cystic cavities located in the projection of the superficial mucosal vessels of different thickness (the so-called "trap" phenomenon) [6,7,8].

The aim of the study was to study the proliferative activity of endometrial hyperplasia in the postmenopausal period.

Material and methods.

The study included clinical and laboratory results of 12 postmenopausal patients who applied to the scientific advisory polyclinic and gynecological department Specialized Scientific and Practical medical center of obstetrics and gynecology with complaints of uterine bleeding.

Immunohistochemical method for detection of antibodies Ki 67, p53, CD138. Ultrasound examination (ultrasound) was performed using Siemens, Aloka, PhilipsHD 3 devices on the day the patient visited the gynecologist of the consultative polyclinic or upon admission to the gynecology department with complaints of AUB, as well as during follow-up for 3, 6 months and 12 months after the onset therapy. During the ultrasound examination of the uterus, the size, structure of the uterus, and the state of the endometrium were evaluated.

When evaluating the endometrium, the following criteria were taken into account:

-thickness, contour of the uterine echo;

- the nature of the external contours of the mucous membrane of the uterine body, the structural features of the endo- and myometrium, the number and size of myomatous nodes.

Formalin-fixed tissues were embedded in paraffin, cut into 4 ҳm sections, and mounted on slides coated with poly-L-lysine. For immunohistochemistry, sections were deparaffinized and rehydrated with descending alcohol grades to distilled water followed by endogenous peroxidase blocking using 3% (v/v) hydrogen peroxidase in phosphate buffered saline (PBS). After that, they were washed in PBS and blocked with mouse serum for 2 hours. Then they were incubated for 30 min with monoclonal antibodies CD138, p53, Ki67 (diluted 1:100). After 3 washes in PBS, sections were incubated with secondary antibody conjugated with peroxidase (1:1000) for 1 hour at room temperature. Immunoreactivity was detected using diaminobenzadine (DAB; Sigma, Germany) to increase sensitivity, with the formation of a brown insoluble precipitate in immunopositive areas. The sections were stained with hematoxylin and mounted on a coverslip. Negative controls were incubated with a solution devoid of any primary antibodies. Immunohistochemical study was carried out by MD. D.A. Nishanov.

The results of the studies were processed using "Lightweight Methods for Statistical Analysis in Clinical Medicine". Statistical processing of the actual material and graphic images were carried out on a Pentium-IV computer.

The results of the study.

Atypical hyperplasia of the endometrium is characterized by the predominance of the glandular component over the stromal component, with a more pronounced and intense proliferation of the glandular epithelium with signs of atypia. The endometrial glands are in large numbers, located close to each other, i.e. compact, the latter of a bizarre and branched appearance.

The basal membrane of the endometrial glands is preserved, they have a narrow layer of connective tissue with fibroblast-like cells, despite their close location "back to back". Some endometrial glands have finger-shaped intussusceptions protruding into their

lumen of the glands.

The epithelium of the glands is single-row, in some places it is multi-row in nature with signs of polarity disturbance, i.e. radial arrangement of cells in relation to the basement membrane. Glandular cells with the presence of hyperchromic enlarged oval nuclei (an increase in the nuclear-cytoplasmic ratio is noted), with varying degrees of mitotic activity, and pathological mitoses are also observed (when examined under high magnification). The stromal component of the endometrium with lymphocytic infiltration of the endometrial stroma, which is focal, and in some places even diffuse.

In the study of scrapings of the uterine cavity in 12 patients with atypical endometrial hyperplasia, it was found that none of the patients had a negative expression of the CD138 antibody.

In 4 (35.0±13.8%) patients, a low reaction was verified, in 3 (25.0±12.5%) patients, an average reaction, and in almost half of the patients, 5 (41.6±14.2%) patients had a high positive reaction. expression of the CD138 antibody.

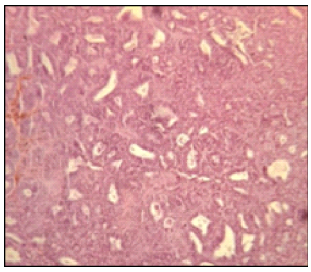

Figure 1. Histological examination. Atypical endometrial hyperplasia.
Staining: Hematoxylin eosin about 10x ok10

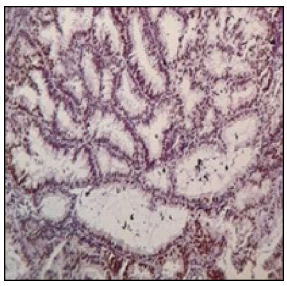

Figure 2. Immunohistochemical study of CD138 antibodies in atypical endometrial hyperplasia Stain: IHC Dab Chromogen. Average positive expression. About 10x ok10.

In the study of the expression of the Ki67 marker in endometrial scrapings with atypical endometrial hyperplasia (diagram 1), it was found that half of the patients - 6 (50%) had an average positive reaction. In every fourth - 3 (25%) patients, the presence of an average expression of the Ki67 marker was verified, and the same high expression - 3 (25%) (Diagram 1, Fig. 1,2).

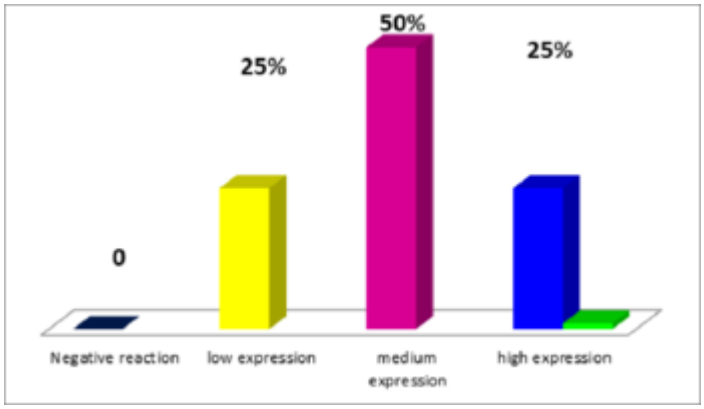

Diagram No. 1 Results of immunohistochemical study of the Ki67 marker in atypical form of endometrial hyperplasia

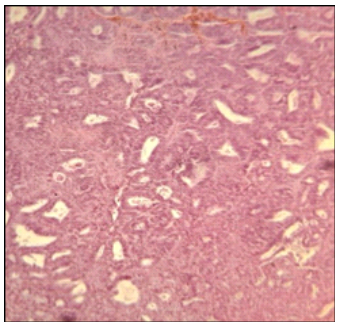

Figure 3. Histological examination. Atypical endometrial hyperplasia.
Stain: Hematoxylin eosin ob 10x ok10

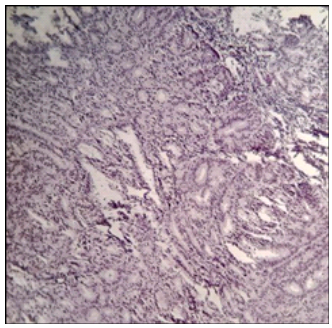

Figure 4. Immunohistochemical study of the Ki-67 marker in atypical endometrial hyperplasia. Stain: IHC Dab Chromogen. Low positive expression. About 10x ok10.

An immunohistochemical study of the expression of the cellular tumor antigen p53 of the endometrium in atypical endometrial hyperplasia in every third 4 (33%) patients revealed a low positive reaction

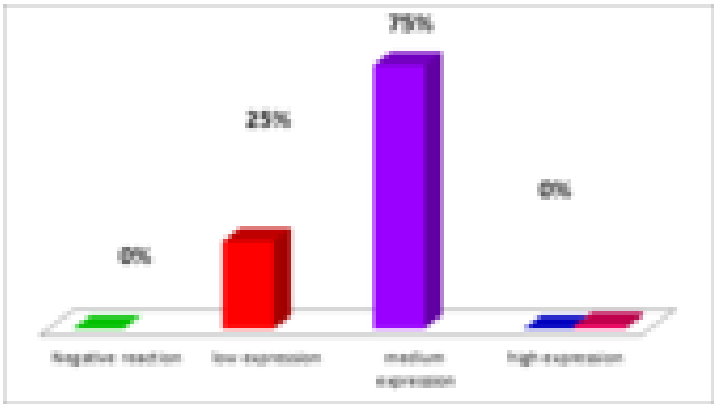

Diagram 2. The results of the study of immunohistochemical parameters of the cellular tumor antigen p53 in atypical form of endometrial hyperplasia.

Every fourth 3 (25.0±12.5%) - low positive expression of the cellular tumor antigen p53. The rest 9 (75.0±12.5%) had a negative reaction, expression of the cellular tumor antigen p53. None of the patients showed high expression of the cellular tumor antigen p53 (Fig. 5, 6).

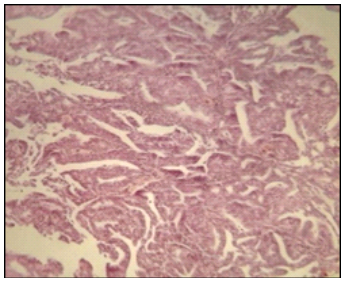

Figure 5. Histological examination. Atypical endometrial hyperplasia.
Stain: Hematoxylin eosin ob 10x ok10.

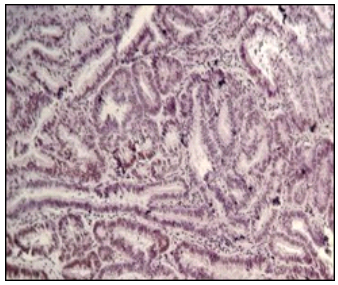

Figure 6. Immunohistochemical study of p53 cellular tumor antigen in atypical endometrial hyperplasia. Stain: IHC Dab Chromogen.Averagepositive expression.About 10x ok10.

Every fourth 3 (25.0±12.5%) - low positive expression of the cellular tumor antigen p53. The rest 9 (75.0±12.5%) had a negative reaction, expression of the cellular tumor antigen p53. None of the patients showed high expression of the cellular tumor antigen p53 (Diagram 2. Fig. 5, 6).

Thus, the obtained results indicate the need for a thorough morphological assessment using immunohistochemical research methods, which largely allows choosing the right tactics for managing such patients. Correctly selected therapy, taking into account some indicators of immunohistochemical markers in AUB against the background of simple endometrial hyperplasia in postmenopausal patients, makes it possible not only to avoid unreasonable surgical interventions, but also to significantly increase the women's health index.

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