

MEDICAL SCIENCES

IMMUNOHISTOCHEMICAL EVALUATION OF ENDOMETRIAL REACTIVITY IN HYPERPLASTIC PROCESSES

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Abstract

In endometrial hyperplasia (EHP), increased proliferative and reactive processes have been detected in the glands and stroma, accompanied by significant changes in the expression of the immunohistochemical markers Ki-67 and CD34. Quantitative analysis revealed that the nuclear expression level of Ki-67 reaches 58%. Such high proliferative index values confirm the active nature of cell division underlying the pathogenesis of EHP during the reproductive period. Analysis of the angiogenesis marker CD34 revealed the presence of intense vascular neoplasms, which is also characteristic of endometrial hyperplasia.

Keywords: endometrium, immunohistochemistry, hyperplastic process, Ki67 and CD34 markers.

Endometrial hyperplastic processes (EHP) including hyperplasia and polyps are histopathological changes in the endometrium resulting from the proliferation of the uterine mucosa, leading to thickening and an increase in its volume. These changes remain the most common gynecological pathology in women of reproductive age. Over the past decades, many researchers have noted an increase in the incidence of EHP, which averages 5-6% of all gynecological morbidity [3, 2, 7, 6].

Particular attention is paid to the study of the molecular biological marker of proliferation, the Ki-67 protein, which is recognized as the most informative and convenient tool for assessing tissue proliferative activity [1, 5]. The study of cell proliferation in various tissue remains one of the fundamental tasks of modern morphology. Thanks to significant advances in molecular biology, morphologists have gained the ability to perform immunohistochemical labeling of cells in various phases of the cell cycle [4].

To evaluate immunohistochemical (IHC) changes in the endometrium in hyperplastic processes using the proliferation marker Ki-67 and the angiogenesis marker CD 34.

Prospective studies of the endometrial function (diagnostic curettage of the uterine cavity) were conducted at two departments of Obstetrics and Gynecology №1 and № 2 of SEI of Avicenna Tajik State Medical University, at Republican Maternity Hospitals № 1

and № 2. The study included 11 reproductive-age patients with hyperplastic pathological processes and a confirmed absence of malignant neoplasms.

For IHC studies, histological sections 2-3 µm thick were stained with special antibodies of Ki-67 and CD-45 markers of the uterine mucosa using the automated system of Ventana Benchmark (Roche, Switzerland). The expression level of markers was assessed quantitatively (as a percentage) and classified as follows: weak expression – up to 20% of positively stained cells; moderate expression – from 20% to 60% of cells; pronounced (strong) expression – more than 60% of cells.

The use of IHC in studying of the endometrium with hyperplastic changes demonstrated a direct correlation between tissue structural changes and its biological potential. The study assessed the expression level of the IHC Ki-67 marker and the proliferative index in the endometrial tissues. It was found that Ki-67 expression is closely linked to the nature of endometrial proliferative disorders. The identified structural changes, such as glandular hyperplasia, were also accompanied by a pronounced positive reaction to the Ki-67 marker. The proliferative index in the Ki-67 was 58%, which corresponds to a high level of cell division and confirms the active pathogenetic nature of the process (Figures 1 and 2).

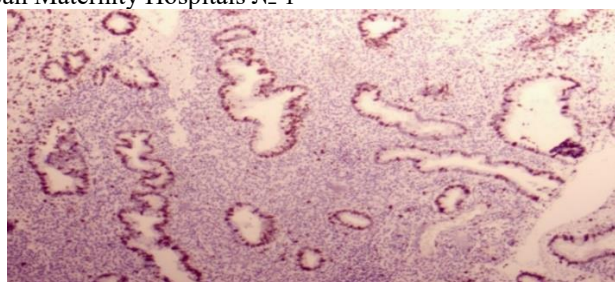


Figure 1. – The degree of expression of the IHC marker Ki-67 in the endometrial glands in HPP. Microphoto. Staining: DAB-hematoxylin. Magnification 50.

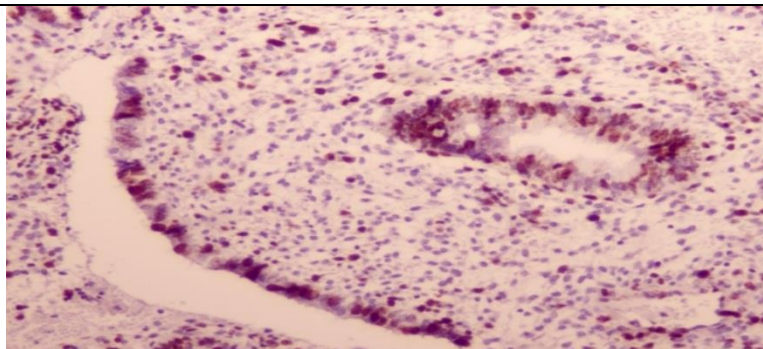


Figure 2. – The degree of expression of the IHC marker Ki-67 in the endometrial glands in HPP. Microphoto. Staining: DAB-hematoxylin. Magnification 100.

The study results showed that the Ki-67 proliferative index was intense in both the glandular epithelium and the endometrial stroma. Morphological analysis revealed that the Ki-67 marker localizes in cell nuclei with varying intensity as distributed between the karyoplasm and nucleolus, corresponding to different phases of the cell cycle. The variability of subcellular localization of Ki-67 confirms its ability to label cells at different stages of proliferation and mitotic activity.

Thus, in the case of EHP, the express level of the Ki-67 marker in the endometrium is 58%. Such high proliferative index values confirm the active nature of cell division, which underlies the pathogenesis of EHP during the reproductive period.

The functional significance of CD 34 and methodological aspects in EHP as a marker of the vasculature, which is a glycoprotein expressed on the surfaces of endothelial cells, making it a reliable marker for the identification of blood vessels. In endometrial studies, CD34 analysis allows for the assessment of the degree of tissue vascularization and the intensity of microangiogenesis in endometrial endothelial cell death. When interpreting staining results, a specific brown precipitate formed during the reaction with DAB indicated positive CD34 expression in the vascular endothelium. The analysis took into account both the signal localization and the staining intensity, reflecting the density of the vascular network in the samples (Figure 3).

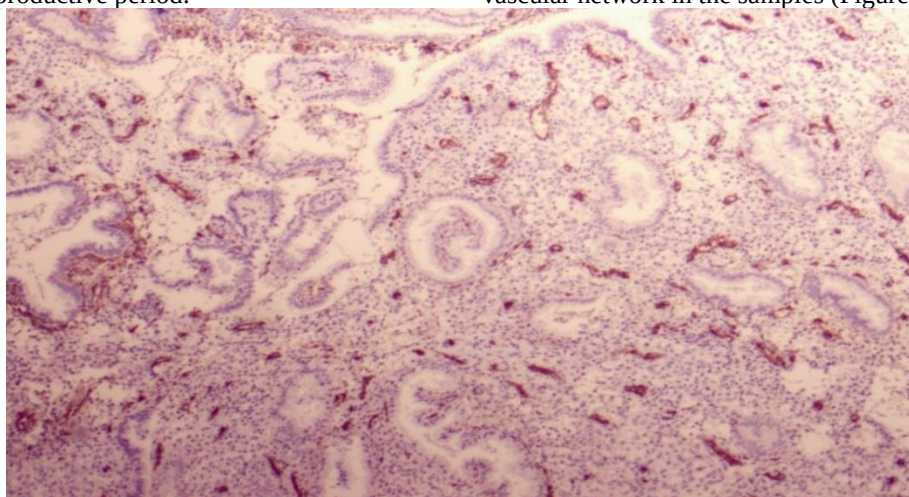


Fig. 3. – Immunohistological examination of CD 34-positive brown blood vessels in the endometrium. The appearance of small spiral arteries is noted. Magnification 50.

The obtained data demonstrate adequate expression of CD34 in endometrial vessels, with clear identification of both small capillaries and larger vascular trunks. Dilation lumen and high vascular density indicate enhanced angiogenesis. Specific brown staining (accumulation of the reaction product with DAB) confirms positive expression of CD34 in vascular endothelial cells.

Microscopic specimens reveal a dense network of exchange vessels and components of the microcirculatory bed. At the level of the terminal vessels of the endometrium, their dilation, tortuosity, and the formation of numerous anastomoses are noted, indicating increased stromal vascularization in this pathology (Figure 3). The study results are consistent with literature data [1,5].

Thus, various variants of endometrial hyperplasia process have diverse immunohistochemical characteristics. High expression of the angiogenesis marker CD34 confirms the intense nature of neovascularization in endometrial hyperplasia.

References:

1. Safarova, S.M. Apoptosis and angiogenesis in diagnostics and tactical selection of treatment of hyperplastic processes [Text] / S.M. Safarova, M.H. Kurbonova, D.B. Sattoroka // Materials of the VII Congress of Obstetricians and Gynecologists of the Republic of Tajikistan. - Dushanbe. - 2022. - p. 283-287.
2. Sviridova, N.I., Tkachenko L.V., Yakhontova M.A., Gritsenko I.A., Maksimov S.N., Puryaseva K.A. Hyperplastic processes of the endometrium: modern

approaches to diagnosis and treatment. *Obstetrics, Gynecology and Reproduction*.-2024; 18(1): 83-95. <https://doi.org/10.17749/2313-7347/ob.gyn.rep.2023.464>

3. Khushvakhtova, E.H. Diagnostic value of various methods of examination of patients of reproductive age with hyperplastic endo-myometrial processes [Text] /, E.H. Khushvakhtova, M.H. Kurbonova, F.M. Akilova // Materials of the VII Congress of Obstetricians and Gynecologists of the Republic of Tajikistan.- Dushanbe.-2022.-p.289-293.

4. Chibisova, G.M., Khabarov, S.V. Kompleksnoe opredelenie onkomarkerov SA125, NE4 i indeksa ROMA kak faktor prognoza razvitya raka yaichnikov [Complex definition of oncoprotein CA125, HE4 and ROMA index as a factor in the prognosis of ovarian cancer]. *Journal of New Medical Technologies*.2018;25(3):15-20/DOI. 10.24411/1609-2163-2018-16158.

5. Khaskhachykh, D.A., Morphological and immunohistochemical characteristics of endometrial layers in women of reproductive age with endometrial hyperplasia without atypia. Scientific digest of association of obstetricians and gynecologists of Ukraine. DOI:10.35278/2664-0707. 2(53).2023.298047.

6. Kossai, M. Penault-Llorca, F. Role of Hormones in Common Benign Uterine Lesions: Endometrial Polyps, Leiomyomas, and Adenomyosis // *Advances in Experimental Medicine and Biology*. – 2020.- № 61.-P. 37-58.

7. Venturella, R. Subcutaneous progesterone for endometrial polyps in premenopausal women: a preliminary retrospective analysis [Text] / R. Venturella, G. Miele, K. Cefali, [et al.] // *J Minim Invasive Gynecol* 2019; 26(1): 143–147.