DIAGNOSTIC SIGNIFICANCE OF THE DETECTION OF PROLIFERATIVE ACTIVITY OF THE CERVICAL EPITHELIUM

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The relevance of research. High mortality, low survival rates of patients due to late diagnosis of cervical cancer requires development of new methods for detecting cancer. According to statistics, this pathology is diagnosed in approximately 500,000 new cases every year, thus there are 14–16 cancer patients with cervical cancer per 100 000 population [3]. The issue of the diagnostic significance of the proliferative activity of the epithelium in the diagnosis of cells and tissues malignancy is now controversial, since the main questions in the pathogenesis of tumors are still unresolved. At this stage of researches the etiological key importance of the human papilloma virus (HPV), trichomoniasis, clamidiosis and other infections in the cervix carcinogenesis is the subject of contentious debates. The issue of the origin of tumor cells is controversial, the malignization of cambial tissue cells and the oncological mutational transformation of the genome are open to question, since transformed cell is immediately came under to apoptosis [4, 10]. The advanced concept of cancer cells circulation in the blood hasn't yet been confirmed. Attempts to treat cancer patients with the injection of HSC programmed differentiation stem cells have been unsuccessful because there is undeveloped and unreasonable conceptual platform under them [7]. The significance of the Ki-67 gene activity in malignancy is now in question [8, 9]. Therefore, at this stage diagnosis and preventive measures, unfortunately, are purely empirical, and sometimes speculative, and they require getting the additional scientific facts. This was the basis for our choice of the scientific research direction. The goal of research was to identify the activity of the Ki-67 gene in diagnosis of the mucous membrane of the cervix pathology in the zone of transition of stratified squamous epithelium into a single-layered cylindrical epithelium against the background of microbial infections in postmenopausal women [6].

Material and methods. The material from postmenopausal women without any inflammatory processes in the mucous membrane of HSC was used as a control in the amount of 5. The material from women against the backgrounds of chlamydial (27), trichomonous (25) and papillomavirus (31) infections was studied in a comparative aspect. We used classical histological methods of staining with hematoxylin and

eosin for obtaining a general morphological pattern, as well as an immunohistochemical method for detecting the proliferation marker of cells - proliferating cell nuclear antigen Ki-67 protein (DAKO, Denmark). The material was analyzed with the Olympus-Bx82 microscope and the PDx82 digital camera with a firmware.

Research results and discussion. The main methods of diagnosis of changes in the cervix were examination in mirrors, simple and extended colposcopy, assessment of vaginal microbiocenosis, cytological examination of impression smears (so-called PAP-smears) and target biopsy followed by histological examination. Given that inflammation of exo- and endocervix can simulate a pattern of cellular atypia during a cytological study, all morphological studies were performed after the sanitation of the vagina. We noted that among women aged 46 years and older ectopia was observed in 7,3% of cases. Sometimes colposcopic pictures can be variegated and combined with a transition zone, but in ectopia of postmenopausal women they didn't have significant differences. It has been established that in the postmenopause the ectopia in the form of focal areas of the cylindrical epithelium was not detected in either case. Sometimes residual effects of ectopia in the form of a transformation zone (TZ) with open and closed glands were observed.

Against the ectopia polyps were found in 2,8% of cases, while in the group of women older than 45 years it was observed in 15% of cases. Polyps more frequently develop at the age of 40-50 years, and recurring of polyps was observed in 18% of patients. Polyp is the proliferation of the mucous membrane of the cervical canal with involvement of the underlying fibrous tissue in this process. The reasons of the polyps' occurrence in the examined patients were associated with a disorder of hormonal and immunogenic homeostasis, and inflammatory processes. Polyps in our observations were less often covered with a cylindrical epithelium, while they had a bright red acinous surface. More often, the polyps were covered with stratified squamous epithelium, in this case they were pink and smooth.

In our researches, when polyps were detected on the uterine cervix, it was noted that this focal proliferation of the stratified squamous epithelium along with the underlying connective tissue with the phenomena of cornification. Externally the papilloma is a pink or whitish verrucose formation. In most cases, the base of the papilloma was broad, less often - in the form of a thin pedicles, and sometimes an external growth was noted. Disorder in the structure of the basal and free plane of the surface epithelium and hyperaemia of the vessels of the proper mucous plate were noted. The basilemma of the epithelium was not identified, leucocytic infiltration was observed not only in the proper mucous plate but also in the lumina of the glands.

Analysis of the proliferative activity of the cervix mucosal epithelium made it possible to establish that, despite the duration of postmenopause, weak proliferative phenomena in stratified squamous and cylindrical epithelium of the cervix can be observed during this period and, respectively, in the first year of postmenopause, proliferative types of smears amount 75%.

In the presence of polyps and inflammatory processes due to chlamydial and trichomonous infections in the cervical mucosa the proliferative activity not only increases in the epithelial plate, but also takes place in its own plate. We noted disorders in the structure of the epithelial plates and lamina propria of the mucous membrane, the disruption of the basilemma, while the daughter cells bloom to the surface of the mucous membrane. It was noted that in case of chlamydial infection the atrophy of the cylindrical epithelium is most franked with the lowest proliferative activity of the epithelium.

Against the age-related estrogen deficiency and overlaying of chlamydial and other infections there are more franked morphological changes associated with epithelial damage, presented as a type of atrophic colpitis (vaginitis) and nonspecific cervicitis. At the same time, there are dystrophic changes in the underlying stroma, associated with worsening of trophicity, decreasing of microcirculation of blood flow and processes of transudation in stroma and all layers in the mucous membranes of the reproductive tract of postmenopausal women. Conclusion report. There are actually no targeted strategies for predicting the fate of cancer of the women's reproductive system now. Sui M., Pei Y., Li D., Li Q., Zhu P., Xu T., Cui M. (2016) as well as other authors note that the delay in diagnosis and treatment can lead to irreversible damage and severe disease [10]. The authors noted that there were rare cases of cervical adenocarcinoma, which is difficult to diagnose because of deep location, endogenous growth, deceptively nonmalignant appearing of the tumor cells and lack of communication with the human papilloma virus (HPV). Liang S.N., Huang Y.J., Liu L.L. et al. (2015) consider that the expression of Ki67 gene is closely associated with the occurrence and development of cervical carcinoma, noting that there is a positive correlation between Ki67 gene and malignancy, and that it can serve as a biomarker for cervical cancer [9].

Kanthiya K., Khunnarong J., Tangjitgamol S., et al. (2016), analyzed the 40-year base of literature data in the evaluation of Ki67 expression in cases of cervical intraepithelial neoplasia (CIN) and cancer, in contrast to the majority of authors who considered

Ki67 expression in 100% of all invasive carcinomas. The analysis results showed 75,4% of the cases of CIN 2–3, 22,6% of the cases of CIN1, and 11,3% of the cases of neoplasia, and obtained a direct association of Ki67 gene activity with the severity of cervical disease especially exhibiting high sensitivity and specificity for CIN2. There was a lack of protein detection in 6 and 7 cases of CIN1 and CIN2, respectively [8].

According to Zhao J., Guo Z., Wang Q., Si T., et al. (2017), the cervical cancer mortality is associated with genotypes of papillomaviruses 16, 18, 58 and 52 [11], but other authors [7,2] consider cytological studies to be more reliable. There were very few large-scale studies dedicated to contamination by the human papillomavirus virus and determination of the dominant type of virus for women in our country. Programs existing at the current stage do not allow assessing the scale of the defeat of women by the human papillomavirus and other infections that occur without vivid clinical symptoms in our country. Nevertheless, the existence of more than 200 strains of human papillomavirus, spontaneous recovery in 98% of cases does not support the advisability of vaccination [5]. The data available at the time indicate the coincidence of prevalence ratios of types 16 and 18 of papillomavirus infection in the Russian Federation and in European countries [2]. High oncogenic types of viruses amount 58% and that fact can alert and explains the high incidence of cervical cancer. The expansion of diagnostic resources, including monitoring of proliferative activity based on analysis and comparative characteristics of regenerative potential indexes in the cervical mucosa with the health model for the corresponding age group, is the most promising in the development of strategies for the prevention, treatment and rehabilitation of postmenopausal women. As in the works of Prilepskaya V.N. (2008), we observed that regardless of the duration of postmenopause weak proliferative phenomena could be in stratified squamous and cylindrical epithelium of the cervix during this period. Our results are consistent with the results of Calil L.N., Igansi C.N., Meurer L., Edelweiss M.I., Bozzetti M.C. (2011), we also found a statistically significant association between cervical mucosa diseases caused by HPVI, Trichomonas, Chlamydia trachomatis and Ki67 gene activity [1]. At the same time, we noted that against the background of a chronic course of infections, the activity of Ki67 gene is statistically significantly reduced which may be due to damage of cambial cells and depletion of the regenerative potential.

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