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MORPHOLOGICAL, PATHOPHYSIOLOGICAL AND MOLECULAR GENETIC FEATURES IN WOMEN WITH BACKGROUND DISEASES OF THE CERVIX

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Relevance: Background diseases of the cervix, especially erosion, refer to diseases with a proven viral bacterial etiology more often as a complication of nonspecific vaginitis and at the same time is a steadily increasing incidence rate. According to WHO data, 617-629 women aged 25-45 annually rank 2nd after breast cancer. Among gynecological diseases occurring in women of reproductive age, the pathology of CMM is from 10 to 15% and is the background for the development of precancerous changes and CMM cancer (CC).

Aim of study of morphological and molecular genetic features in women with background diseases of the cervix.

Materials and methods of research. Examinations of 46 women of reproductive age with an active sexual life from 25 to 45 years old who applied for a gynecological examination were conducted.

Results. According to the results of the study, it was found that no hyper methylation of genes was detected in 30 patients, and none of them also revealed precancerous changes and breast cancer.

Keywords: cervicitis, vaginitis, vaginal suppositories, turmeric oil

Introduction. Every year, about 500,000 primary patients with breast cancer are registered in the world, which, being in most cases preventable, is the cause of death of 250,000 women per year. There are background and precancerous diseases, cancer in situ and common breast cancer. Background CMM diseases, especially recurrent ones, serve as predisposing factors in the development of precancerous changes and breast cancer. In this regard, the study of both benign and precancerous diseases is of great importance for the prevention of breast cancer [1]. Currently, the key concept of the etiopathogenesis of breast cancer is the viral hypothesis, according to which the main exogenous factor of cervical carcinogenesis is HPV. The action of viral genes only initiates the tumor process, but is insufficient for its progression. HPV infection is a key moment in the early stages of carcinogenesis in CMM and a determining factor for triggering subsequent genetic processes leading to the formation of a monoclonal population of tumor cells. Tumor growth may be preceded by the appearance of diffuse changes in the form of dystrophy, atrophy, hyperplasia and dysplasia, which lead to the restructuring of organ structures and disrupt secretory and other functions of the

epithelium. Epithelial dysplasia is recognized as a marker of the initial stages of the malignant process. Dysplastic epithelium is characterized by the inability of cells to carry out the normal maturation process [2, 3, 4].

Aim of study of morphological and molecular genetic features in women with background diseases of the cervix.

Materials and methods of research. Examinations of 46 women of reproductive age with an active sexual life from 25 to 45 years old who applied for a gynecological examination were conducted. All patients underwent a comprehensive morphological and immunohistochemical study of the cervical tumor. Morphological examination of paraffin sections stained with hematoxylin and eosin was carried out.

To clarify the condition of CMM, all patients underwent extended colposcopy. At the beginning of the study, a simple (overview) colposcopy was performed, and a Schiller test was performed to identify clearer colposcopic patterns. In case of deviation from the normal colposcopic picture, cytological examination of scrapings from the surface of the CMM and the cervical canal was performed. Curettage of the cervical canal was performed in a hospital under intravenous anesthesia on the 5th-7th day of the menstrual cycle with a mandatory histological examination of the obtained surgical material. Determination of molecular oncological markers in CMM biopsies and endocervix scrapings was carried out in the Scientific Laboratory of the Republican Research Center of Oncology and Radiology of Bukhara. [5,6].

Results. According to the results of the study, it was found that no hypermethylation of genes was detected in 30 patients, and none of them also revealed precancerous changes and breast cancer. Abnormal gene methylation was detected in 16 patients in the biopsy materials: p16 – in 94, MLH1 – in 81% of cases. Depending on the histological diagnosis, the following frequency of distribution of abnormal gene methylation was observed. In CMM leukoplakia, methylation of the p16 gene was noted in 83% of cases and MLH1 in 66%, the same frequency of methylation of these genes was recorded in CMM dysplasia samples – in 100% of cases, with squamous cell carcinoma, 100% of patients had methylation of the p16 gene (Table 1).

Table 1. Frequency of hypermethylation of p16, MLH1 genes in CMM tissues according to histological diagnosis data

Diagnosis	Number of patients (%)		
	p16	MLH1	Total
Leukoplakia	5 (82)	4 (68)	9 (100)
Dysplasia of CMM	8 (64)	8 (36)	16(100)
RSM	1 (50)	1 (50)	2 (100)

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Cytological examination of scrapings from the surface of the CMM and the cervical canal was performed in all patients. Cytological examination of patients with cervical ectopia revealed intermediate and parabasal cells of multilayered squamous epithelium, glandular epithelial cells, as well as separately located nuclei, leukocytes, erythrocytes. Patients with leukoplakia revealed a large number of non-nuclear cells of the squamous epithelium, separate scales and their clusters that covered all fields of vision, as well as metaplastic cells, signs of dyskariosis. The following pattern is characteristic of CMM dysplasia: cell nuclei are significantly enlarged, hyperchromia of the nuclei is pronounced, the lesion occupies half of the epithelial layer, intercellular connections are weakened, cell maturation is disrupted. Cytoplasm of cells – of varying degrees of maturity. According to the results of cytological diagnostics, in smears taken from CMM, in patients without abnormal gene methylation, cylindrical epithelial cells were most often detected (n=11), signs of leukoplakia (n=7) and dysplasia phenomena (n=9) were observed. Cells of normal multilayer epithelium were detected in 3 patients (Table 2).

Table 2. Frequency of detection of abnormal gene methylation in CMM tissue samples depending on the results of cytological diagnostics

Cytological diagnostic data	Number of patients (%) total hypermethylation		
	total	no	there is
Normal cells of the cylindrical epithelium	13	11 (85)	2 (15)
Signs of dysplasia	17	9 (53)	8 (47)
Normal cells of the multilayer squamous epithelium	3	3 (100)	–

Histological examination of CMM biopsies in patients with established abnormal gene methylation revealed a picture of simple leukoplakia (n=2), signs of chronic inflammation (n=2), squamous cell carcinoma (n=2), grade II–III dysplasia (n=7), phenomena of coilocytosis (n=2), cervical ectopia (n=1). The data are presented in Table 3.

Table 3. Frequency of detection of abnormal gene methylation in CMM tissue samples with its various pathologies

Histological diagnosis	Number of patients (%) hypermethylation		
	total	no	there is
Leukoplakia	7	5 (71,5)	2 (28,5)
RSM	2	–	2 (100)

Dysplasia CMM	10	3 (30)	7 (70)
The phenomena of inflammation, cervicitis	11	9 (82)	2 (18)

Thus, a high frequency of hypermethylation of the p16 (100%), ML HI (100%) genes was established in CMM tissue samples with a confirmed histological diagnosis of dysplasia and relapse of the disease in the form of leukoplakia.

Conclusion. Based on the data obtained, it can be assumed that the detection of abnormal methylation of the p16, N33 and MLH1 genes in CMM tissue samples may indicate the presence of a potential risk of precancerous changes and breast cancer. Determination of gene hypermethylation in CMM biopsy materials is associated with a probable risk of recurrence of CMM diseases. At the same time, the absence of methylation can serve as a favorable prognostic sign regarding the risk of recurrence of CMM diseases.

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