CERVICAL CANCER DURING PREGNANCY (MODERN ASPECTS OF DIAGNOSIS AND SCREENING)

[1]Tugizova Dildora Ismoilovna, [2]Amelie Nushofarin Bezhanovna
Samarkand State Medical University

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Abstract. *Cervical cancer is the most common type of gynecological cancer during pregnancy; and in recent years, according to foreign authors, its frequency is 1.5-12 cases per 100 thousand pregnancies. The relevance of the combination of malignant tumors with pregnancy is primarily due to the delay in childbearing. Thus, in 2014, the average age of Russian women at the birth of a child was 28.1 years, in contrast to 24.9 years in 1995. It is in this age group (25-29 years) that cervical cancer occupies a leading position (19.17%) among all oncological diseases. Diagnosis of cervical cancer in pregnant women today remains not fully understood and controversial.*

Keywords: *cervical cancer, cytological screening, colposcopic screening, immunocytochemical studies, targeted biopsy.*

Cervical cancer ranks first among pregnancy-associated gynecological tumors and, according to various authors, is detected on average 0.8-1.2 per 10,000 pregnancies [1,2]. Cervical cancer detected within 6 months after termination of pregnancy and 12 months after delivery is classified as a pregnancy-associated tumor because clinical and morphological manifestations of the tumor process are already present during pregnancy. Urmancheeva et al. believe that, among patients with cervical cancer, the frequency of combination with pregnancy is 1-3%. The average age of patients with cervical cancer in combination with pregnancy is 30 years [13,15].

Foreign literature data indicate that the incidence of cervical cancer in recent years is 1.5-12 cases per 100 thousand pregnancies [1].

The relevance of the combination of malignant tumors with pregnancy increases every year. This is primarily due to the delay in childbearing. In the last decades, the share of cervical cancer among young women has occupied a leading position. The Demographic Yearbook of Russia indicates that, in 2014, the average age of Russian women at the birth of a child was 28.1 years, as opposed to 24.9 years in 1995. [Demographic Yearbook of Russia, 2015]. According to A.D. Caprina in 2016 in Russia in the age group of 25-29 years, cervical cancer occupies a leading position (19.17%) among all cancers, ahead of lymphoproliferative diseases and breast cancer, and at the age of 30-34 years, the proportion of cervical cancer uterus is also high (23.76%), leaving this tumor in first place among all cancers in young people [Kaprin A.D., 2018].

According to some foreign authors, cervical intraepithelial neoplasia (cervical intraepithelial neoplasia , CIN) II, III degree, Ca in situ , equated according to the modern classification to severe dysplasia (HSIL, high grade squamous intraepithelial lesions), is a preinvasive cervical cancer with a risk of progression to an invasive process in pregnant women from 1.1 to 3.6% [Kärrberg C., 2013,]. The prevalence of CIN among pregnant women, in contrast to invasive cervical cancer, is higher and is 13.0 cases per 10,000 [Al-Halal H., 2013]. A significant increase in the detection of CIN in pregnant women is associated with more careful monitoring and examination of pregnant women when they are registered. Despite the early

detection of the preinvasive form of cervical cancer in pregnant women, neglect is often diagnosed.

The reasons for the neglect of cervical cancer in pregnant women are: the lack of research when taking pregnant women into the dispensary or preparing them for artificial termination of pregnancy; in the presence of bloody discharge from the genital tract, the cervix is \u200b\u200bnot examined, smears are not taken for cytological examination; misinterpretation of the clinical manifestations of cervical cancer during pregnancy; fear of a biopsy from the eroded vaginal part of the cervix during pregnancy; incorrect sampling of material without colposcopic control; lack of oncological alertness in patients with precancerous changes in the cervix. This requires a more in-depth study of the diagnosis of cervical cancer in the early stages.

The prevalence of cervical intraepithelial neoplasia (CIN) in the population of pregnant women is approximately 1% [5]. According to the literature, in recent years, cytological examination has been recommended as a routine method of examination during pregnancy, since most lesions of the cervix occur in young women of childbearing age [4]. The effectiveness of cytological screening has been proven, this method is the "gold standard" for the prevention and diagnosis of dysplasia and cervical cancer. After an abnormal cytological picture has been detected during cytological screening, a number of examinations should be recommended to pregnant patients, such as visual examination of the cervix using mirrors, cytological examination, colposcopy . A number of authors believe that diagnostic procedures should not differ from those in non-pregnant women. (3)

According to foreign experts, observation during pregnancy of a group of patients with CIN (verified cytological) should be carried out with regular gynecological examinations, including Pap smear, colposcopy and targeted biopsy (if indicated). The American Society for Colposcopy and Cervical Pathology recommends that if abnormal squamous cells of uncertain significance or cells with mild squamous intraepithelial lesions (CIN 1) are detected in pregnant women , colposcopy should be delayed for up to 6 weeks . postpartum, since the probability of detecting CIN 2-3 in these cases postpartum is only 3.7% [6]. If there is no evidence to support the presence of cervical cancer, no treatment should be given during pregnancy and all therapy may be delayed until the postpartum period. In patients with cancer in situ and with a microinvasive process without any changes, monitoring is recommended: colposcopy in any trimester, if progression is suspected, modified cervical conization should be performed [3].

A number of authors believe that if a malignant tumor of the cervix is suspected according to a cytological examination , it is advisable to perform a morphological examination of the cervical tissue as a stage of in-depth diagnostics. At the same time, several methods for collecting material for histological examination are considered, such as colposcopy -guided targeted biopsy , multiple quadrant biopsy, and modified conization of the cervix [7].

Most clinicians recommend limiting themselves to multiple needle biopsies, which have little to no complication potential. However, with this biopsy technique, there is a significant frequency of erroneous conclusions - from 6 to 25% [7]. Given such a large number of errors in a simple biopsy, another group of researchers is of the opinion that conization is appropriate , but not in the classical version. During pregnancy, the transition zone of the cervical epithelium usually shifts towards the vaginal part, therefore, a cone depth of 1.5 to 2.0 cm is sufficient, in places of 3.0-3.5 cm. But a cone-shaped biopsy during pregnancy, especially in the early stages

and after 34 weeks _ pregnancy, may be accompanied by severe complications: significant bleeding, miscarriages, premature births (from 5 to 25%).

To date, recommendations for screening and diagnosis of cervical cancer during pregnancy are clearly defined. Pap cytology of the cervix should be performed during the first prenatal visit to the doctor. Further management tactics will depend on the result of the cytological examination. In the presence of LSIL (low grade squamous intraepithelial lesion , mild squamous intraepithelial lesion) in a smear, cytology and colposcopy are performed 6–8 weeks after delivery, with HSIL (high grade squamous intraepithelial lesion , severe squamous intraepithelial lesion) the patient is referred for colposcopy . Biopsy of the cervix is performed

only with suspicion of cervical cancer, both cytologically and colposcopically . Endocervical curettage during pregnancy is contraindicated [1]. In cases where the results of the study of biopsy material confirm the presence of invasive cervical cancer, further management tactics patients are discussed collectively, together with oncologists.

Intervention for CIN during pregnancy is dangerous due to the threat of its termination, while delaying treatment may carry the risk of progression of the disease.

In her works, E. A. Verbitskaya reported that cytological examination is an effective method for diagnosing and monitoring CIN associated with pregnancy. The sensitivity of the method was 97.9%. Immunocytochemical study (ICC) of "double staining" is an additional method in the diagnosis and prognosis of the course of CIN (in all cases of a negative result of ICC "double staining", regression of the disease was observed after childbirth.

Verification of the diagnosis and cytological monitoring were carried out by methods of traditional and liquid cytological examination of the exo- and endocervix epithelium . Qualitative signs of proliferative and antiproliferative activity markers Ki -67 and p16 in CIN in pregnant women were studied using immunohistochemical and immunocytochemical methods.

An important diagnostic criterion for CC is the association with HPV. Using the polymerase chain reaction method, the frequency of human papillomavirus (HPV) infection among women with CIN in combination with pregnancy was revealed.

Recent studies have revealed a trend towards an increase in the incidence of HPV among pregnant women to an average of 31%, while among non-pregnant women this figure does not exceed 18%. [22]. In the literature, it is noted that from the 1st to the 3rd trimester, the frequency of HPV detection increases to 46%, and then sharply decreases after childbirth. This can be explained by the fact that a change in the hormonal background of a woman affects the degree of virus replication, while the frequency of cell atypia does not increase .

Thus, given the high information content of the cytological study, there is no need to perform a conibiopsy for histological confirmation of the diagnosis during pregnancy. CIN detected during pregnancy is not an indication for abortion. For CIN , treatment can be delayed, but cytological monitoring during pregnancy and postpartum is necessary to detect progression.

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