Algorithm For Examining Pregnant Women With Cervical Pathology To Exclude Cancer

Yakubbekova Sokhibahon Sadik kizi

Associate Professor of the Department of Oncology
Andijan State Medical Institute
Andijan, Uzbekistan

ABSTRACT

Cervical cancer is the most common malignancy associated with pregnancy. The management of patients with this disease is a unique and complex clinical situation, due to the unpredictable behavior of the tumor during pregnancy and the impossibility of performing all necessary diagnostic and therapeutic measures.

It is impossible to perform all necessary diagnostic and therapeutic procedures. Pregnancy is a factor that triggers tumor development due to hormonal changes, decreased immune defenses, improved blood and lymph flow to the reproductive organs, and postpartum cervical changes. Diagnosing cervical cancer during pregnancy is particularly challenging due to the high risk of under- or overdiagnosis, as well as the unavailability of many diagnostic methods. When examining patients, it is necessary to carefully differentiate between normal and pathological growth processes during pregnancy.

Keywords: Pregnancy, cervical cancer, CIN, human papillomavirus

Relevance. Cervical cancer (CC) remains a pressing issue in gynecologic oncology. It is the leading cause of gynecologic oncology and has a growing incidence [1]. It is noteworthy that 45.4% of all cases occur in women under 50 years of age. Furthermore, CC is known to be the most common malignant neoplasm associated with pregnancy. The incidence of this pathology ranges from 1 to 13 cases per 10,000 pregnancies. The average age of affected pregnant women is 30 years, suggesting that late childbirth and a late first pregnancy may be factors triggering tumor development [2, 3].

The management of patients with this pathology is a unique and complex clinical situation, due to the unpredictable behavior of cervical tumors during a developing pregnancy and the impossibility of performing all necessary diagnostic and therapeutic measures. Choosing a treatment strategy is extremely challenging; therapy is individualized and depends on a number of factors, such as the stage of the disease, the gestational age at the time of tumor detection, the condition of the fetus, and the patient's desire to maintain the pregnancy [1].

Cervical cancer is a disease of the female reproductive system characterized by the development of a malignant neoplasm on the cervix. The main histological subtype is squamous cell carcinoma (SCC), occurring in almost 85% of patients, while cervical canal involvement occurs in 10–15% of cases [4].

The most significant factor in the development of cervical cancer is HPV infection [5]. It is important to note that the development of cervical intraepithelial neoplasia (CIN), a precancerous condition, is often independent of pregnancy. However, the risk of HPV infection increases due to increased sensitivity of the cervical epithelium to the pathogen and changes

in the immune system aimed at maintaining pregnancy.

The risk factors for developing the disease in pregnant and non-pregnant patients are the same: frequent changes of sexual partners, early onset of sexual activity, and neglect of barrier contraception. All of these

factors increase the risk of infection with the HPV virus, the replication of whose DNA and associated capsid proteins, in particular the oncoproteins E6 and E7, alter the cell cycle and lead to cellular atypia, which is the basis for the development of CIN and, as a consequence, cervical cancer. An important role in the pathogenesis of the neoplastic process is the ability of the virus to inhibit the functions of the oncoprotector p53, which leads to the induction of proliferative processes [4, 6]. In addition, according to modern studies, pregnancy contributes to the progression of malignancy and, in some cases, can induce the development of cervical cancer between changes in the levels of estrogens, progesterone and human chorionic gonadotropin (hCG) and HPV infection (types 16 and 18) [7, 8].

The risk of metastasis in squamous cell carcinoma is 0.8%, and in adenocarcinoma, 1.5% [9]. Increased growth rates of existing tumors and accelerated metastasis processes are associated with physiological changes in the female reproductive system: decreased immune defenses in early pregnancy, improved blood flow and drainage of the lymphatic system in the reproductive organs, and changes in the condition of the cervix after childbirth [7].

Cervical cancer detected within 6 months after termination of pregnancy, as well as 12–18 months after childbirth, is classified as a pregnancy-associated neoplasm, due to the fact that morphological and clinical manifestations of this pathology can already be detected during pregnancy [10]

Materials and methods. The clinical group included 22 pregnant women with cytologically detected CIN III and AC. Targeted biopsy was performed in 12 pregnant women after extended colposcopy with diagnosis verification: Ca in situ (5 cases), leukoplakia with atypia (3 cases), CIN III associated with flat condyloma (4 cases). In 10 cases, biopsy was not necessary, as colposcopic images of increased atypical epithelium were not detected. Additional testing included PAP smear, cervical curettage, and HPV screening with viral load. Adequate diagnostic tactics allowed patients not only to preserve their desired pregnancy but also allowed physicians to refrain from unnecessary biopsies, given the competent interpretation of cytocolposcopic and PCR data. For all patients with a verified diagnosis, treatment in the form of electroexcision for therapeutic and diagnostic purposes was carried out 1.5 months after delivery, which made it possible to finally clarify the extent of the pathological process and assess the adequacy of the treatment and diagnostic tactics.

Results. Given the relevance of this problem, we have developed and implemented in clinical practice a diagnostic algorithm for identifying cervical pathology in pregnant women. Stage I: initial examination upon registration of the pregnant woman: bacteriological (Femoflor-screen), virological (HPV screening with viral load), extended colposcopy, PAP test. Stage II: allocation of groups of pregnant women depending on the identified cervical pathology, dynamic colposcopic and cytological monitoring if CIN-Ca in situ is detected once every 12 weeks. A cervical biopsy during pregnancy is performed in the presence of atypical cytological and colposcopic images suspicious for cancer (heterogeneous surface, lumpy leukoplakia, exophyte, atypical vascularization). Endocervical curettage is also performed if indicated.

According to studies, early pregnancy is considered safe, since CIN1 regresses in most cases, but progresses in 30% of cases under the influence of hormonal changes [11]; with CIN2 and CIN3, progression is observed in 50% of cases. Therefore, treatment of CIN1 can be postponed until 6 weeks after delivery; with CIN2 and CIN3, regular examination of pregnant women is recommended to exclude the development of cervical cancer. If disease progression is suspected, a repeat biopsy is recommended [7]. Usually, such patients undergo organ-preserving conization of the cervix after delivery [11]. Treatment of patients

with stages IA2 and IB1 and tumors up to 2 cm before 22 weeks of pregnancy begins with atypical conization of the cervix with lymphadenectomy. The purpose of this operation is to determine the stage of the disease. If metastatic lesions of the lymph nodes are detected, termination of pregnancy is recommended [9]. However, according to ESCO (European Society of Clinical Oncology), pregnancy can be preserved if neoadjuvant chemotherapy is started immediately, followed by radiation and chemotherapy in the perinatal period [7]. Pregnancy preservation is possible in the absence of lymph node metastases. Postpartum treatment is carried out according to the standard regimen [9].

The management of patients with IA2 and IB1 after 22 weeks of pregnancy and with tumors up to 2 cm also begins with atypical conization of the cervix, but pelvic lymphadenectomy is not performed, since it is impossible at this stage; if IA2 is confirmed, treatment is carried out according to the standard regimen; with IB1, lymph node involvement, neoadjuvant polychemotherapy is preferred, regardless of the presence or absence of IA2 [7, 9].

If tumors larger than 2-4 cm are detected before 22 weeks of pregnancy in IB1, pelvic lymphadenectomy should be performed to determine the stage of cervical cancer. If histological examination reveals lymph node metastases, a decision should be made to terminate the pregnancy and standard treatment should be administered. If the lymph nodes are normal, pregnancy can be prolonged with neoadjuvant polychemotherapy after 12 weeks of pregnancy [9].

CONCLUSION

Thus, the average age of affected pregnant women was 30 years, suggesting that late childbirth or delayed first pregnancy may be a factor in the development of neoplasia. Altered levels of estrogen, progesterone, hCG, and HPV infection, decreased immune defenses, improved lymphatic blood flow and drainage of the reproductive organs during pregnancy, and cervical dilation in the postpartum period contribute to tumor progression. The similarity between the growth process during pregnancy in normal and pathological conditions complicates diagnosis due to the high risk of misdiagnosis.

In our view, only the joint efforts of gynecological oncologists and primary care obstetricians/gynecologists will enable the timely and objective diagnosis of dysplastic changes and early cervical cancer in pregnant women, preventing the development of invasive forms.

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