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Case Report

Unveiling the uncommon: invasive adenocarcinoma cervix presenting during pregnancy: a rare case report

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ABSTRACT

Adenocarcinoma of the cervix presenting during pregnancy is an exceedingly rare occurrence, and the optimal management approach remains uncertain due to limited reported cases. Here we are presenting a case of a multiparous lady who presented with complaints of amenorrhoea for 3 months, pain abdomen, spotting per vaginum, mass felt per vaginum. Ultrasonography showed single live intrauterine pregnancy at 11 weeks 4 days of gestational age with an ill-defined hyperechoic lesion measuring 4.36×4.92×4.16 cm in cervix. HPE of cervical biopsy confirmed cervical adenocarcinoma-endocervical type, grade 2. On MRI, a heterogeneous exophytic irregular mass involving the external os, protruding into the upper vaginal cavity was identified with infiltration into the anterior upper vaginal wall, pelvic lymphadenopathy, and sub-centimetric inguinal lymph nodes were observed. The patient underwent radical hysterectomy with bilateral pelvic lymph node dissection. The surgical specimen exhibited stromal invasion exceeding 5mm in depth and width greater than 7mm, involving entire cervical wall with lympho-vascular space invasion. The tumor was ER/PR negative, strongly positive for P16, and HPV studies were also positive. Adjuvant external beam radiotherapy (EBRT) was administered to the pelvis, and the patient is currently in remission.

Keywords: Adenocarcinoma cervix, Intrauterine pregnancy with cancer, Human papillomavirus

INTRODUCTION

Pregnancy complicated with cervical cancer refers to cervical cancer diagnosed during the current pregnancy as well as cases diagnosed 6-12 months after delivery. The incidence of pregnancy complicated with cervical cancer is low. About 1%-3% of women diagnosed with cervical cancer are pregnant or postpartum at the time of diagnosis.^{1,2} About one-half of these cases are diagnosed prenatally, and the other half are diagnosed in the 12 months after delivery.³ Cervical cancer is one of the most common malignancies in pregnancy, with an estimated incidence of 0.8 to 1.5 cases per 10,000 births.³⁻⁶ Adenocarcinoma of the cervix presenting during pregnancy is an exceedingly rare occurrence, and the optimal management approach remains uncertain due to limited reported cases.⁷

Whether pregnancy can accelerate the progression of cancer is still controversial. Some scholars have found that the levels of estrogen, progesterone, and human chorionic gonadotropin during pregnancy are positively correlated with human papillomavirus (HPV) 16 and HPV 18 infection, which indirectly suggest that pregnancy may promote the progression of cervical cancer.⁸ Some studies have shown that the lymphatic circulation and blood flow of the reproductive organs of pregnant women increases, the immunity of the body decreases in the early stage of pregnancy and cervical dilation after delivery, and other factors may accelerate the metastasis of tumors, thereby accelerating the development of cervical cancer.⁹ Here is a unique case of invasive cervical adenocarcinoma diagnosed in a pregnant woman, shedding light on the challenges and considerations in such situations.

CASE REPORT

A 32-year-old G9P7017 at 11 weeks 5 days of period of gestation presented with complaints of amenorrhoea for 3 months, pain abdomen, spotting per vaginum, mass felt per vaginum. On, per speculum examination ~5×5 cm cauliflower growth was seen arising from the cervix which bleeds on touch. Ultrasound examination showed single live intrauterine pregnancy at 11 weeks 4 days of gestational age with an ill-defined hyperechoic lesion measuring 4.36×4.92×4.16 cm in cervix. HPE of cervical biopsy confirmed cervical adenocarcinoma-endocervical type, grade 2. On further imaging via MRI, a heterogeneous exophytic irregular mass involving the external OS and protruding into the upper vaginal cavity was identified. Additionally, infiltration into the anterior upper vaginal wall, pelvic lymphadenopathy, and sub-centimetric inguinal lymph nodes were observed. The patient underwent radical hysterectomy with bilateral pelvic lymph node dissection 17 days after the initial presentation. The surgical specimen exhibited stromal invasion exceeding 5 mm in depth and a width greater than 7 mm, involving the entire cervical wall with lympho-vascular space invasion. The tumor was found to be ER/PR negative, strongly positive for P16, and HPV studies were also positive. Adjuvant EBRT was administered to the pelvis, and the patient is currently in remission.

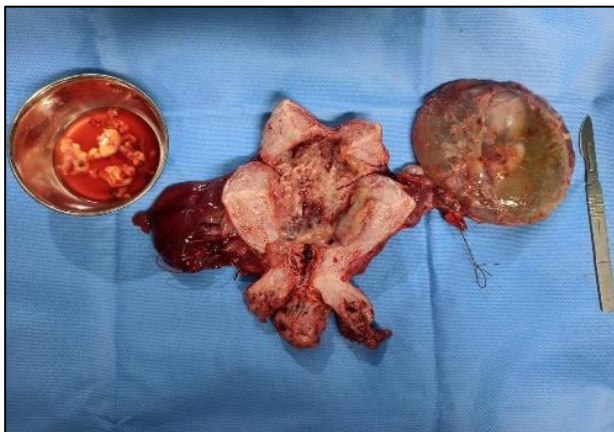


Figure 1: Hysterectomy specimen with cervical mass with intrauterine amniotic sac with foetus with dissected lymph nodes.

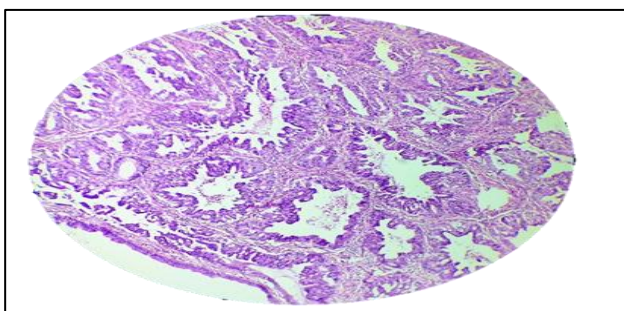


Figure 2: Adenocarcinoma cervix-high power microscopy.

DISCUSSION

Cervical cancer is the most frequent malignancy diagnosed during pregnancy and fortunately most patients are diagnosed at an early stage. Management of cervical cancer during pregnancy depends on a number of factors such as the stage of disease (tumor size), lymph node involvement, duration of pregnancy, histological subtype, the patient's desire to continue the pregnancy, and desire for future childbearing.¹⁰

Cervical cytology is the first choice for rapid diagnosis of cervical cancer. The test does not pose a threat to mothers and children throughout pregnancy. Previous studies have shown that the accuracy of cervical cytological diagnosis in pregnancy is similar to that in nonpregnancy.¹⁰⁻¹² However, recent studies have shown that changes in maternal estrogen and progesterone levels lead to glandular hyperplasia of cervical mucosa, migration of squamous-columnar junction, active proliferation of basal cells, irregular cell morphology, and enlargement of nuclei, which are easily misdiagnosed as highly squamous intraepithelial lesions or even invasive cancer.⁸⁻¹⁰ In view of the specificity of the cervix during pregnancy, it is recommended that cervical cytology smears be made by experienced pathologists who can then examine and make a conclusion on the film to reduce misdiagnosis.¹¹

Cervical biopsy will not increase the incidence of complications during pregnancy, abortion rate, and premature delivery rate, but curettage of cervical canal during pregnancy will increase the abortion rate and premature delivery rate.^{12,13} Therefore, this procedure is forbidden during pregnancy. In addition, the cervix during pregnancy is prone to bleeding. If the site of biopsy is too large or too deep, it can cause massive bleeding or even abortion. To minimize these risks, some scholars have proposed that the depth of biopsy should be less than 1 cm, and the biopsy should not be too large, so that bleeding can easily be stopped (if any).⁸

The treatment of pregnancy with cervical cancer has not been well established yet, neither in China nor abroad; however, it can be treated according to the clinical stage and whether the pregnancy will be allowed to progress or will it be terminated. If pregnancy is to be terminated, the treatment is the same as that of nonpregnant women with cervical cancer. For those patients maintaining their pregnancy, specific treatment can be combined with cervical cancer staging, tumor size, gestational weeks, fetal development, and pelvic lymph node involvement.

Standard treatment for patients with locally advanced cervical cancer remains chemotherapy and radiation. Since radiation therapy may be associated with spontaneous abortion, congenital malformations, and paediatric malignancies it is not routinely recommended during pregnancy. An expectant management may be feasible for patients already near term, as foetus has already reached lung maturity and the risk of perinatal morbidity is low.

Neoadjuvant chemotherapy has emerged as an alternative to concurrent chemotherapy and radiation, and it may offer patients the option to delay definitive treatment until foetal viability. In this setting, platinum-based chemotherapy is the most frequently used systemic therapy in pregnant women.¹⁴

The effect of chemotherapy on the fetus depends on the dose of drugs transferred to the fetus by pregnant women receiving chemotherapy during pregnancy. Calsteren et al studied placental transport of chemotherapeutic drugs commonly used in pregnant baboon models.¹⁵ The results showed that the average concentration of carboplatin in baboon fetal plasma was 57.5% of the maternal body; in addition, the concentration of paclitaxel in fetal umbilical cord blood was 15% of the maternal body after 3 hours of paclitaxel infusion; after transfusion of docetaxel, the concentration of docetaxel in fetal umbilical cord blood was 5%-50% of maternal plasma, while after 26 hours, the concentration of both was high. The transplacental transmission rate of trastuzumab decreased from 85% to 3% at 2 and 26 hours after trastuzumab injection. Kohler et al suggested that there might be a platinum placental filtration mechanism because the platinum concentrations in fetal cord blood and amniotic fluid were 23%-65% and 11%-24% of maternal blood, respectively.¹⁶ Chemotherapy can directly act on the growing fetus, or indirectly act on the growing fetus through the placenta.^{17,18} After the development of fetal organs, chemotherapy can affect fetal eyes, genitals, hematopoietic system, and central nervous system.¹⁷ Chemotherapy-induced suppression of maternal and fetal bone marrow can also lead to anemia, which in turn affects fetal growth.¹⁹

CONCLUSION

The clinical manifestations of pregnancy complicated with cervical cancer are atypical, easily confused with pregnancy diseases, easily concealed by pregnancy status, and difficult to diagnose. Prenatal examinations are often neglected by pregnant women, which make it difficult to detect tumors. Invasive adenocarcinoma of the cervix during pregnancy presents a unique clinical challenge. This case underscores the need for a comprehensive understanding of diagnostic modalities, timely intervention, and a multidisciplinary approach to ensure effective management and favourable outcomes for both the mother and the developing foetus. In the choice of treatment plan, we should consider both fetal and maternal factors. Conditional hospitals can set up a multidisciplinary consultation (MDT) team. Combining the clinical stages of patients, lymph node status, histological types of tumors, gestational weeks, imaging data, patients and their families' willingness to pregnancy, we can weigh the advantages and disadvantages and formulate individualized treatment plan. It is the best choice for pregnancy complicated with cervical cancer. Currently, there is no uniform standard for treatment. Further research and the accumulation of similar cases are

essential to inform evidence-based guidelines for the management of cervical adenocarcinoma in pregnant individuals.

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