CASE REPORT
UDC: 618.146-006:612.63:616.071:615-085

Arch Oncol 2005;13(3-4):145-7.
DOI: 10.2298/AOO0503145M

Microinvasive cervical cancer in pregnancy

Ljiljana Mladenović Segedi[1], Petar Novaković[2], Aljoša Mandić[2], Olgica Mihajlović[2], Tatjana Ivković-Kapicl[2]

ABSTRACT

Cervical cancer is the most frequently diagnosed malignant disease in pregnancy. The clinical symptoms are scarce or none. The diagnosis is made primarily with a cervical smear, as well as a colposcopic examination and directed cervical biopsy. The treatment of cervical cancer depends on the stage of the disease, the gestation period, and a patient's wish to carry a pregnancy to term. The illustrated case is of a patient who with the diagnosed presence of microinvasive squamous cell cancer, due to cervical biopsy, in the 1st trimester of pregnancy. In the 2nd trimester, diagnostic conization was performed in order to exclude the presence of the invasive disease. The definite histopathologic findings indicated the presence of cancer in situ. The conization margins were negative and thus the patient was successfully cured. The patient had a cesarean birth in the 36th week of pregnancy and she gave birth to an alive female newborn. Women are given the chance to have cervical cancer diagnosed and treated in the early stages of pregnancy owing to the introduction of a cervical smear in the modern protocol of antenatal protection.

[1]Gynecology and Obstetrics Clinic, Novi Sad, [2]Institute of Oncology Sremska Kamenica, Serbia & Montenegro, Address correspondence to: Assist. mr sc. med. Ljiljana Mladenović-Segedi, Gynecology and Obstetrics Clinic, 21000 Novi Sad, Branimira Ćosića 37, Serbia & Montenegro, E-mail: ljiljaseg@eunet.yu, The manuscript was received: 03. 10. 2005, Provisionally accepted: 19. 10. 2005, Accepted for publication: 22. 11. 2005

KEY WORDS: *Pregnancy; Cervix Neoplasms; Diagnosis; Neoplasm Staging; Treatment Outcome*

INTRODUCTION

Cervical cancer, one of the most common cancer in women's reproduction period, is the most frequently diagnosed malignance during pregnancy (1, 2). The median age of cervical cancer diagnosed in pregnancy has been reported to be 30 to 35 years of age. Reports from tumor registries and large maternity hospitals throughout the world show an overall incidence of cervical cancer in pregnancy ranging from 7.5 to 45.0 cervical cancers per 100,000 pregnancies (1,3,4).

Should only women in their fertility period be taken into consideration, the combination of cervical cancer and pregnancy is found in up to 10% of the cases (5,6).

There is a strong causal relationship between the HPV (human papillomavirus) infection and the presence of the displastic lesions of the cervix and cervical cancer. HPV is nowadays considered the primary cause of the beginning of cervical cancer. The existence of the DNA sequence of HPV virus is proved in more than 93% of all cervical cancers (7). Except for the HPV infection, there are many other contributive factors: smoking, the use of oral contraceptives (in connection with sexual behavior), young age at first sexual intercourse, having numerous sexual partners, a high number of childbirths, the first childbirth at an early age, the consumption of certain vitamins such as carotenoid, vitamin C and folic acid, the presence of other sexually transmitted diseases, and the decrease in humoral and cellular immunity (8-10).

The symptoms of the presence of cervical cancer in pregnancy are the same as with women who are not pregnant. Vaginal bleeding is the most common (43%-54%), while 30% to 50% of pregnant women experience no symptoms whatsoever (11). Diagnosis is based on an examination of the cervix and on taking a cytological cervical smear, colposcopic findings; and if necessary a targeted cervical biopsy. The stage of the disease during pregnancy is also defined according to FIGO classification. The most frequent histological type of cervical cancer in pregnancy, as well as in not pregnant women, is squamous cell carcinoma (80%); less frequently is cervical adenocarcinoma (about 11%) (1).

Cervical cancer is curable if it is diagnosed and treated on time i.e., in its early stages. There is a significant dilemma about the treatment of cervical cancer in pregnant women. The treatment depends on the stage of the disease, but also on the patient's age i.e. on the ability of the fetus to survive outside the uterus at that moment. The wish of a patient to carry pregnancy to term can also significantly postpone the treatment and consequently its outcome and result. Optimum outcome of the treatment would mean: a) preserving the life of a pregnant women, b) optimum cure of the malignant disease, c) protecting the fetus as well as the newborn baby from potentially harmful effects of the treatment, d) preserving a woman's procreation ability (12).

CASE REPORT

In July 2004, a 27 years old woman came for a gynecological examination in the 14th week of pregnancy. The case history then taken was that she had been feeling well, and that during her previous pregnancy, in January 2002, she had been diagnosed as having cervical ectopy and the presence of koilocytes in the class II cervical smear. At that time, HPV typing had not been done. Six weeks later, a repeated cervical smear was again class II, so the patient was suggested that she should have a check-up six weeks after the childbirth. She gave a vaginal birth to a male newborn whose birth weight was 3350 g. However, the

patient did not go for a suggested check-up.

In the 10th week of the pregnancy in question, she began bleeding and thus went to a gynecologist. The examination showed the presence of ectopy with atypical vascularization. A cervical smear taken was class III. Upon biopsy, she was diagnosed as having microinvasive squamous cell carcinoma.

With this diagnosis, she was sent to the Institute of Oncology in Sremska Kamenica. After hospitalization, a gynecological examination was done and following findings were obtained: the outer genitals - without changes; the vagina - penetrable with two fingers, soft, elastic walls, livid; the cervix - cylindrical, the orificium closed, papillary ectopy around the orificium 3 x 3 cm; the uterus - normal uterus size for the time of pregnancy, soft, without contractions; the adnexa bilateral - without changes. The preoperative ultrasound findings were: the normal quantity of amniotic fluid, the placenta at the posterior wall of the uterus, BPD: 47.5 mm, THQ: 41.6 mm, FL: 28.7 mm, the fetus's heart beat and movement were registered. Based on the decision of the oncology commission, conization of cervix was performed and a cervical cerclage in the 18/19th week of pregnancy. There were no operative and immediate postoperative complications. The postoperative ultrasound findings were: normal structure of the placenta at the posterior wall, the normal quantity of amniotic fluid, the fetus's spine and limbs of normal findings, the umbilical cord with three blood vessels inside of it, BPD: 45.7 mm, FL: 27.9 mm, the fetus's heart beat and movement were registered. The patient was given a tocolytic therapy perorally (Ritodrine tablets) and was discharged on the day 7 after the operation. The patient's general state of health was satisfactory. She had to continue with the therapy and was advised to go on regular check-ups. The pathologist has analyzed 37 H&E stained slides from cervical excision materials (from a cone biopsy of the cervix). Based on morphologic criteria, carcinoma in situ was detected in 9 cervical tissue samples. There was no evidence of penetration of basement membrane. Endocervical and exocervical margins were not involved (Figure 1, 2).

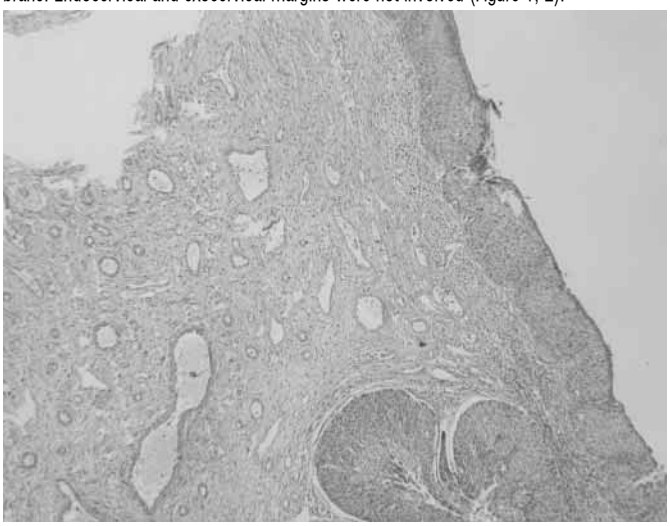

Figure 1. Cervical in situ squamous cell carcinoma. (H&E, magnification 5x10)

The pregnancy continued without any problems until the week 33/34, when the patient was brought to the Obstetrics and Gynecology Clinic, in Novi Sad, due to profound bleeding. She was examined upon the hospitalization and the findings obtained were: a small amount of spotting in the vagina, the presence of a cervical cerclage after conization. There were visible contractions of the uterus during the examination. The patient was given an intravenous tocolytic therapy (Fenoterol ampule, No II in 500 ml of 5% glucose IV) and a corticosteroid therapy (Dexamethasone 4 x 6 mg IM). The complete lab test was done. On the second day of the hospitalization, she was also administered ceftriaxone 2 x 1 g IM due to fever (the

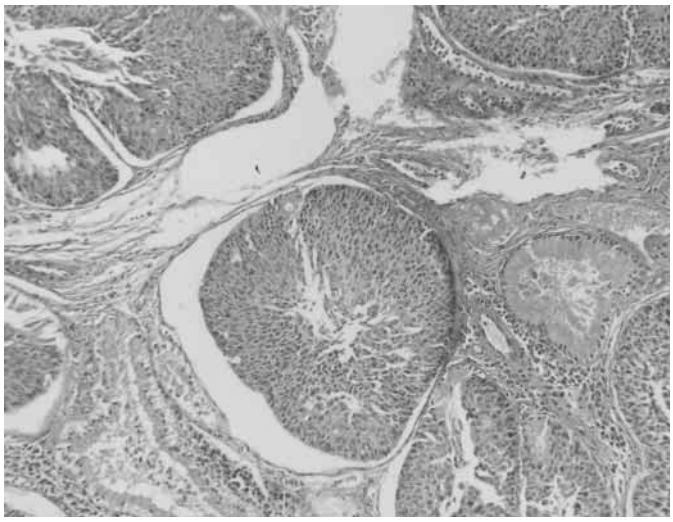

Figure 2. In situ cervical squamous cell carcinoma. (H&E, magnification 10x10). Endocervical glands entirely replaced by atypical squamous cells, circumscribed with intact basal membrane

patient's temperature was 38ºC). Her urine, cervical smear, vaginal fluids, and throat and nose smear were taken for the bacteriological examination. On the day 4 of the antibiotic therapy, the patient developed the allergic reaction to Ceftriaxone. The findings of bacteriological examination of urine were positive (isolated Enterococcus species) and thus gentamicin a 120mg, 2x1 amp IM was added to the therapy. The other lab results were normal, and the results of all the smears negative. A cervical smear result was class II.

The findings of the ultrasound examination of the fetus were: BPD 8 mm, FL 63 mm, HC 300 mm, AC 319 mm, the placenta at the anterior wall of the uterus, placental maturity stage II, the normal quantity of amniotic fluid. The estimated weight of the fetus was 2500 g. The fetus's left kidney was polycystic.

Despite the tocolytic therapy (which was administered perorally but also intavenously when the contractions were stronger), the patient continued having contractions; and thus had a cesarean birth in the 36th week of pregnancy. She gave birth to an alive female newborn whose birth weight was 3060 g. After the birth, Apgar score was 7/9. On day 2 of the postoperative recovery, the patient's temperature raised up to 38ºC, so the antibiotic therapy was continued. She was discharged on the 5th postoperative day. Her general state of health was satisfactory. Due to its prematurity, the baby was sent to the Institute for Health Protection of Children and the Young in Novi Sad.

Four months later, the patient came on a regular gynecological check-up. A cervical smear was taken with class II result.

DISCUSSION AND CONCLUSION

Early pregnancy gives a unique opportunity for diagnosing premalignant and malignant disease of cervix. A woman's suspicion that she may be pregnant is a reason for going to a gynecologist. One part of a routine examination in early pregnancy is a specula examination for cervix visualization and taking a cervical smear, from both ecto- and endocervix, for the cytological examination, apart from a bimanual palpatory examination and an ultrasound for fetus viability. Taking ecto- and endocervical smear for cytological examination is the most important in a diagnosis. A patient with abnormal test results of a cervical smear has to undergo a colposcopic examination. In most cases, this examination during pregnancy enables the visualization of the complete area of transformation because of the eversion of the squamocolumnar junction, which is a normal physiological process happening in the first trimester of pregnancy. Colposcopy is rather difficult in pregnancy, even for an experienced gynecologist, because of the physiological changes of the cervix resulting from the activity of the hormones. It is necessary to have a good knowledge of physiological

processes in order not to diagnose as suspicious something that it is not (13,14).

When colposcopic findings are abnormal or when there is a suspicion of invasive cancer, it is necessary to perform a targeted biopsy. Colposcopy and a targeted biopsy during pregnancy are exact and accurate methods of the examination of a pregnant woman who has abnormal cervical cytology findings. There is a good correlation between colposcopic and histopathological findings in pregnancy (14).

Conization as a diagnostic - therapeutic method is performed during pregnancy only in extremely selective cases because of possible complications that can jeopardize both a mother and her fetus. As a result, the performance of conization is necessary only in the case of unsatisfactory coloscopic findings and there is a suspicion of an invasive cancer. Equally so, if the results of the biopsy indicate the presence of microinvasion it is necessary to perform conization in order to exclude the presence of invasive cancer. Conization during pregnancy is performed only as a diagnostic method owing to a high percentage of positive conization margins and a residual disease. The described incidence of a residual disease after conization during pregnancy is up to 50% (14).

Complications resulting from conization in pregnancy can be various. Postoperative bleeding occurs in about 55 to 14% cases, bearing in mind that the risk increases with the progress of pregnancy. Miscarriage occurs in 3 - 6%, however, if conization is performed in the 1st trimester, the risk is higher i.e. 33 - 50% (15). Owing to above mentioned, it is recommended to postpone conization to the 2nd trimester even if the illness was detected in the 1st trimester of pregnancy. In that case cervical stenosis, PROM, intrauterine infection or a premature birth occur more seldom (16).

The biopsy of the patient above mentioned indicated the presence of microinvasive cancer. Conization was performed to eliminate existence of invasive cancer and than performed the cerclage. The definite histopathological findings showed the presence of cancer in situ and that the change had been removed leaving the satisfactory thickness of the healthy tissue around the cancer. The majority of authors agree that the definite treatment of in situ and microinvasive cancer based on the histopathological verification (biopsy and conization) can be delayed to after childbirth.

It appears that pregnancy-associated cervical carcinoma has an overall better prognosis than in the non-pregnant population due to the relatively high proportion of patients with early stage disease. After stratifying for stage, survival analyses generally do not show a difference between the two groups (17). Due to diagnostic and therapeutic difficulties associated with it in pregnancy, re-evaluation after delivery is crucial. Our patient had a cesarean birth, although the latest data in medical literature suggests a possibility of vaginal birth in cases of cervical in situ cancer (3,12,18).

However, the risks of obstructed labor, hemorrhage and episiotomy site recurrence with vaginal delivery has led to the recommendation of caesarean delivery as the preferred method (19).

REFERENCES

1. Method WM, Brost BC. Management of cervical cancer in pregnancy. Semin Surg Oncol 1999;16:251-60.
2. Tewari K, Cappuccini F, Freeman RK, DiSaia PJ. Managing cervical cancer in pregnancy. Contemp Obstet Gynecol 1999;44:134-45.
3. Hacker NF, Berek JS, Lagasse LD, Charles EH, Savage EW, Moore JG. Carcinoma of the cervix associated with pregnancy. Obstet Gynecol 1982;59:735-46.
4. Duggan B, Muderspach LI, Roman LD, Curtin JP, d'Ablaing G 3rd, Morrow CP. Cervical cancet in pregnancy: reporting on planned delay in therapy. Obstet Gynecol 1993;82:598-602.
5. Jones WB, Shingleton HM, Rissel A, Fremgen AM, Clive RE, Winchester DP, et al. Cervical carcinoma and pregnancy. A national patterns of care study of the American College of Surgeons. Cancer 1996;77:1479-88.
6. Creasman WT, Rutledge FN, Fletcher GH. Carcinoma of the cervix associated with pregnancy. Obstet Gynecol 1970;36:495-501.
7. Richart RM. Causes and menagement of cervical intraepithelial neoplasia. Cancer 1987;60(8 Suppl):1951-9.
8. zur Hausen H. Human papillomaviruses in the pathogenesis of anogenital cancer. Virology 1991;184:9-13.
9. Yoo KY, Kang D, Koo HW. Risk factors associated with uterine cervical cancer in Korea: a case-control study with special reference to sexual behaviour. J Epidemiol 1997;7:117-23.
10. Mandelblatt J. Squamous cell cancer of the cervix, immune senescence and HPV; is cervical cancer age-related neoplasm? Adv Exp Med Biol 1993;330:13-26.
11. Norstrom A, Jansson I, Andersson H. Carcinoma of the uterine cervix in pregnancy. A study of the incidence and treatment in the western region of Sweden 1973 to 1992. Acta Obstet Gynecol Scand 1997;76:583-9.
12. Pavlidis NA. Coexistence of pregnancy and malignancy. Oncologist 2002;7:279-87.
13. Economos K, Perez Viridiano N, Delke I, Collado ML, Tancer ML. Abnormal cervical cytology in pregnancy: a 17-year experiance. Obstet Gynecol 1993;81:915-8.
14. Baldauf JJ, Dreyfus M, Ritter J, Philippe E. Colposcopy and directed biopsy reliability during pregnancy: a cohort study. Eur J Obstet Gynecol Reprod Biol 1995; 62:31-6.
15. Allen DG, Planner RS, Tang PT, Scurry JP, Weerasiri T. Invasive cervical cancer in pregnancy. Aust N Z J Obstet Gynaecol 1995;35:408-12.
16. Hannigan EV, Whitehouse HH 3rd , Atkinson WD, Becker SN. Cone biopsy during pregnancy. Obstet Gynecol 1982;60:450-5.
17. Sood AK, Sorosky JI. Invasive cervical cancer complicating pregnancy. How to manage the dilemma. Obstet Gynecol Clin North Am 1998;25:343-52.
18. Zemlickis D, Lishner M, Degendorfer P. Maternal and fetal outcome after invasive cancer in pregnancy. J Clin Oncol 1991; 9:1956-61.
19. Lishner M. Cancer in pregnancy. Ann Oncol 2003;14 Suppl 3:iii31-6.