

CHEMOTHERAPY AND CESAREAN SECTION FOLLOWED BY RADICAL SURGERY IN LOCALLY ADVANCED CERVICAL CANCER DURING PREGNANCY

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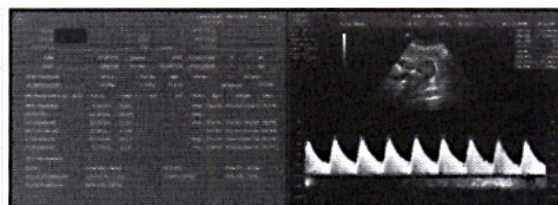
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Reference chart of fetal biometry

Introduction: Cervical carcinoma is the second most common gynecological malignancy during pregnancy with incidence of about 0,05%. Its management depends on gestational age at the time of diagnosis, stage of disease, woman's desire to continue the pregnancy and her desire to preserve fertility. Cervical cancer detected in the first trimester is treated by radical hysterectomy or by radiotherapy. Cervical malignancy detected during the third trimester is treated surgically after delivery of the baby by cesarean section. The management of the disease diagnosed in the 2nd trimester remains controversial and difficult.



Reference table of fetal biometry

Dopplerometry of umbilical artery

CASE REPORT A 30-year-old woman in the 24th week of pregnancy presented at our institution with complaints of vaginal bleeding. Gynecologic examination, vaginal sonography and magnetic resonance imaging (MRI) revealed cervical tumour 43 x 32 mm large with no parametrial or vaginal involvement. Histological examination confirmed invasive, well-differentiated squamous cell carcinoma. Ultrasound examination revealed intrauterine pregnancy with normal fetal anatomy. Due to strong patient's desire to continue the pregnancy, neoadjuvant chemotherapy with weekly cisplatin at dose of 40 mg/m² of body surface area regimen was started in order to prevent disease progression. In total 7 doses of chemotherapy were administered between 25th and 31st week of pregnancy with no adverse effects on fetus and with no signs of toxicity to the patient. The disease was restaged and evaluated for objective response and operability based on gynecologic examination, transvaginal sonography and control MRI in the 33rd week of pregnancy. After a course of antenatal steroids, an elective cesarean section followed by radical Wertheim-Meigs hysterectomy and pelvic lymphadenectomy with no residual macroscopic disease and no intraoperative complication were performed at 34th week of pregnancy. Lymphatic mapping procedure with combined sentinel node detection was performed intraoperatively. The postpartal adaptation of the 2070 g female newborn with Apgar score 9/10/10 was complicated by artificial pneumothorax and the need of endotracheal ventilation but the newborn was discharged 19 days later in good condition. The patient's postoperative course was uneventful. Histopathological evaluation showed residual tumour 14x10mm large, no lymphovascular invasion and no metastases in all 34 lymphnodes. Four weeks postpartum the patient started three-cycle adjuvant cisplatin and ifosfamid chemotherapy regimen repeated every 3 weeks for the total period of four months. Six months after the treatment the patient is in good condition without any signs of recurrence.



Conclusion: The result of our case and results of other published studies prove good responsiveness of cervical carcinoma in pregnant woman to chemotherapy, low toxicity in maternal organism and no adverse effect on fetus such as hematotoxicity, neurotoxicity or intrauterine growth restriction. The use of chemotherapy in locally advanced cervical carcinoma treatment during pregnancy results in significant tumour regression and may be considered as a promising therapeutical approach. Only few cases of neoadjuvant chemotherapy during pregnancy have been reported. As the safety of chemotherapy can not be proved in large, well designed, prospective studies there is a need of individual approach, especially in patients in 2nd trimester of pregnancy with stage IB2 cancer, who are highly motivated to preserve their pregnancy. A longer follow-up of the cases is needed to determine the possible long-term negative effect of the chemotherapy on the child.

Discussion: The first report about the use of chemotherapy during pregnancy is from Jacobs et al. in 1981 for an oat cell carcinoma of the cervix. Therapy comprised of a single injection (50 mg/kg) of cisplatin at 10 week's amenorrhea followed by a radical hysterectomy 2 weeks later.

Giacalone et al in 1996 published a very similar report of one case with cisplatin-based neoadjuvant chemotherapy in a woman who refused to terminate her pregnancy. Treatment comprised of a single agent therapy with cisplatin for 3 cycles of 75 mg per m² body area. There was a complete clinical response after three cycles of chemotherapy. At 32 weeks, a cesarean section with radical abdominal hysterectomy with pelvic and paraaortic lymphadenectomy were performed. During the follow-up of the newborn there were no signs of any metabolic or hematologic abnormality.

Tewari et al in 1998 reported two patients with locally advanced cervical carcinoma diagnosed early in the second trimester that were treated with neoadjuvant chemotherapy until the third trimester, and then underwent delivery and final surgical treatment. The tumour in both patients responded by dramatic reduction of the volume, making radical hysterectomy possible at the time of cesarean section. In addition, both patients tolerated chemotherapy well and there were no adverse fetal effects. Favourable neonatal outcomes were achieved. One patient experienced recurrence within 5 months of surgery, whereas the other patient remained disease free for 2 years.

Marana et al in 2000 published a case of a woman with FIGO stage IIB squamous cell cervical carcinoma at 15 weeks of gestation, treated by primary chemotherapy with cisplatin and bleomycin, until delivery at 38 weeks. At the time of publication, the child was already 3 years old and had no signs of any development abnormalities.

A case report from Bader et al. in 2006 describes a woman with FIGO stage IIA cervical cancer who received four cycles of cisplatin (50 mg/m²) and vincristine (1 mg/m²) at 3-weeks interval starting at 23 weeks of gestation. A cesarean section with radical hysterectomy and pelvic lymphadenectomy were performed at 33 weeks, delivering a 1920 g male newborn. Histology showed a poorly differentiated squamous cell carcinoma with lymphovascular invasion and pelvic lymphnode metastases. The patient received three further cycles of chemotherapy. Both mother and child are healthy at 80 months after the initial diagnosis was set.

A case report of Caluwaerts et al. in 2006 describes a woman with stage IB1 invasive squamous cervical cancer treated with six cycles 75 mg/m² cisplatin every 10 days starting at 17th week of pregnancy. An elective cesarean delivery followed by radical hysterectomy and lymphadenectomy were performed at 32 weeks of gestation. The pathological examination revealed a moderately differentiated squamous cell carcinoma of 3,5 cm and all 33 lymph nodes were free of disease. Infant's examination did not reveal any development abnormalities until 6 month after birth.

Karam et al. in 2007 reported a case of a woman at 23 weeks gestation with poorly differentiated stage IB2 squamous-cell carcinoma of the cervix with MRI imaging suggestive of parametrial and rectovaginal septal involvement. She received neoadjuvant chemotherapy using weekly cisplatin from 24th to 30th weeks. At 33 weeks a cesarean section followed by radical hysterectomy, bilateral pelvic and para-aortic lymphadenectomy and bilateral ovarian transposition were carried out, followed by adjuvant concurrent chemoradiation.