

Magnetic resonance imaging for the treatment planning in invasive carcinoma of the cervix in pregnant women

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Purpose. To evaluate magnetic resonance imaging (MRI) in the planning of optimal treatment- radiotherapy or radical surgery in pregnant patients with invasive carcinoma of the cervix.

Material and methods. Four patients with invasive carcinoma of the cervix in pregnancy underwent MRI for evaluation of the tumor extent with an emphasis on parametrial invasion and pelvic lymph node metastases. In all 4 patients the diagnosis of carcinoma of the cervix was established in the first trimester of pregnancy.

Results. Clinical stage IB was confirmed in two patients, IIB in one patient and IA in one patient. The first patient with stage IB disease was treated with radical Wertheim's hysterectomy. The second patient with stage IB was found inoperable due to bladder involvement not revealed by the MRI. This patient was subsequently treated with radiotherapy. The microscopic examination confirmed deep infiltration of the cervical stroma as detected by preoperative MRI in the radically operated case and the presence of metastases to the pelvic nodes in both patients, also detected by MRI.

The third patient with stage IIB disease was treated with external beam irradiation to the pelvis and intracavitary brachytherapy. In the course of follow-up ranging from 9 to 35 months one patient recurred in the paraaortic region and was subsequently treated with surgery and adjuvant chemotherapy.

Conclusion. MRI is a useful tool for noninvasive staging of pregnant patients with invasive carcinoma of the cervix. All data suggesting a subclinical spread of the tumor outside the cervix may be helpful in selecting the optimal method of treatment.

Ocena przydatności magnetycznego rezonansu jądrowego w diagnostyce inwazyjnego raka szyjki macicy współistniejącego z ciążą

Cel. Celem pracy była ocena przydatności magnetycznego rezonansu jądrowego w planowaniu leczenia chorych na inwazyjnego raka szyjki macicy, współistniejącego z ciążą oraz w monitorowaniu nowotworu w przypadku odroczenia terapii.

Materiał i metody. U 4 chorych z potwierdzonym mikroskopowo inwazyjnym rakiem szyjki macicy, współistniejącym z ciążą, wykonano MRI miednicy w celu oceny stopnia zaawansowania nowotworu.

Wyniki badania obrazowego skorelowano ze stanem klinicznym i na tej podstawie dwie chore z nowotworem w stopniu IB oraz jedną w stopniu IIB poddano natychmiastowemu leczeniu onkologicznemu – chirurgii lub radioterapii. W jednym przypadku, z uwagi na rak naciekania podścieliska szyjki macicy, zarówno w ocenie MRI, jak i biopsji, podjęto decyzję o planowym odroczeniu leczenia do rozwiązania ciąży i porożu.

Wyniki. Analiza porównawcza wyników oceny mikroskopowej oraz MRI przypadków operowanych potwierdziła wysoką zgodność w zakresie oceny głębokości naciekania zrębu szyjki macicy oraz stanu regionalnych węzłów chłonnych miednicy.

Wnioski. Wczesne doświadczenia własne potwierdziły wysoką wartość diagnostyczną rezonansu magnetycznego w przypadkach raka szyjki macicy, współistniejącego z ciążą. Możliwość wykrycia szerzenia się procesu nowotworowego poza szyjkę macicy w fazie przedklinicznej pozwala na optymalizację leczenia, a w szczególnych sytuacjach umożliwia planowe odroczenie terapii do momentu rozwiązania ciąży.

Key words: cervix cancer, pregnancy, magnetic resonance imaging

Słowa kluczowe: rak szyjki macicy, ciąża, rezonans magnetyczny

Introduction

Invasive carcinoma of the cervix complicating pregnancy is a rare clinical entity. The estimated rate of this malignancy ranges from 0.3 to 0.5% of live deliveries [1].

This particular clinical situation is highly challenging for the treating team. The optimal therapeutic decision can be made after a very careful consideration of all important prognostic factors of the tumor, age of pregnancy and the will of the pregnant woman. The diagnosis of invasive cervical cancer in early pregnancy warrants immediate treatment inevitably leading to fetal loss. There are, however, women who place such a high value on pregnancy, that they are willing to undertake the risk of delaying the treatment until the fetus is mature. This very personal decision requires counseling by the gynecologist-oncologist and obstetrician regarding the risks both to the fetus and the mother.

Accurate staging is the main determinant in managing patients with cervical cancer and has been estimated by the clinical FIGO staging system. However, the discrepancy between clinical staging and surgical staging is found in 17 to 32% of patients with stage IB disease. The inaccuracy of clinical staging is even more apparent in pregnant patients due to hyperaemia and oedema of the pelvic tissues.

Recent reports show the superiority of MRI over clinical staging [2-5]. A relative lack of teratogenic effect of MRI even after repeated examinations and high tissue resolution make this imaging technique optimal for pre-treatment evaluation of pregnant women with invasive carcinoma of the cervix [2].

In this report the authors present their preliminary experience with the use of MRI for pretreatment evaluation and management of carcinoma of the cervix in pregnant women.

Material and methods

Between 1998 and 2001 four pregnant women with carcinoma of the cervix were admitted to Department of Gynecological

Oncology of the Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology in Warsaw for pre-treatment evaluation or definitive therapy. In all cases the diagnosis was established in the first trimester – between the 6th and the 11th week of pregnancy. After a routine staging workout including clinical examination and abdominal ultrasound the diagnosis of stage IA (FIGO) was established in 1 case, IB in two cases, and IIB in one case. For further confirmation of the stage of the disease in all patients pelvic MRI examination was carried out using a Philips Gyroscan ACS-NT 1.5T with the following imaging parameters: T1/TSE/512; TE 14ms; TR 500ms; NSA 6 acquisitions
T2/TSE/512; TE 150ms
STIR; TE 100ms; TR 1800ms; TR 150ms; NSA-3

The images were obtained in the frontal, sagittal and transversal projection.

For the contrast enhanced images Gd-DTPA with the dose of 0.2 ml/kg was administered.

In the MRI evaluation of pregnant women with carcinoma of the cervix special attention was paid to the following prognostic parameters: depth of cervical infiltration, parametrial or vaginal involvement, rectal or bladder involvement and pelvic lymphnode status.

Figures 1 and 2 present a MRI image of stage IB cervical cancer in a pregnant woman and the surgical specimen.

After completing the staging procedure one patient with stage IB disease was treated with radical Wertheim-Meig's

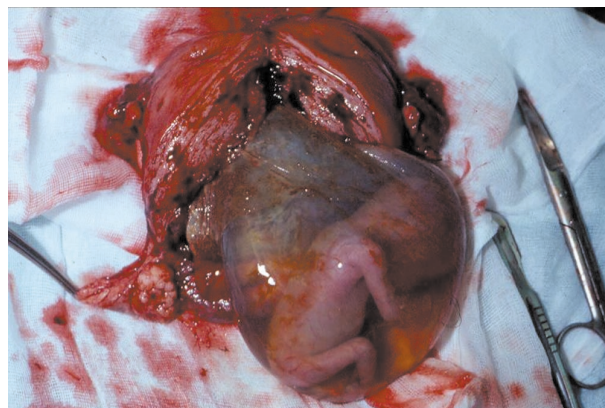


Figure 1. Surgical specimen presenting the transected uterus with cervical infiltration and the foetus

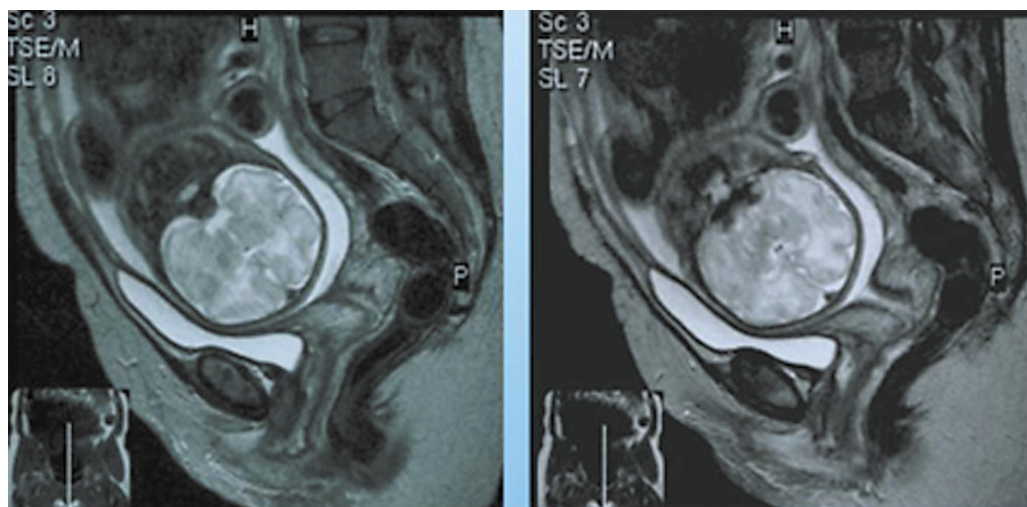


Figure 2. T2 image of pregnant uterus with cervical infiltration of the tumor

hysterectomy, while the second patient with clinical stage IB confirmed by MRI underwent laparotomy. In this case radical hysterectomy had been abandoned due to infiltration of the bladder. The patient subsequently underwent a course of chemoradiotherapy with the dose of 50 Gy to the pelvis with weekly cisplatin 30 mg/kg. The third patient with stage IIB disease was treated with radiotherapy consisting of pelvic external beam irradiation to the dose of 45 Gy and intracavitary brachytherapy Cs.137/LDR with the dose of 40 Gy in the reference point A. The fourth patient with stage IA disease was followed up to the term delivery. Definitive treatment in the form of amputation of the cervix was carried out 6 weeks postpartum.

All patients were followed up regularly after completion of the treatment for 12, 16, 18 and 30 months.

Results

After a pretreatment staging work-out stage IB invasive carcinoma of the cervix was diagnosed in two cases, IIB in one case and IA in one case.

In subject one MRI revealed an infiltrate of the cervix with the diameter of 30 mm with a deep infiltration of the cervical stroma of more than 50% of its thickness. The stromal ring at MRI had the thickness of 3 mm, suggesting uninvolved parametria. There was no sign of pelvic lymphadenopathy. The patient underwent radical hysterectomy at the 15th week of gestation. The pathologic specimen confirmed the existence of a tumor measuring 27x16x18 mm. Both parametria and the vaginal cuff were free of the tumor. The pelvic nodes were also negative for metastases.

The second patient had a stage IB disease diagnosed at the 9th week of gestation. MRI showed a bulky tumor of the cervix with the diameter of 38x22x18 mm with no obvious parametrial involvement or pelvic lymphadenopathy. The patient was referred for radical hysterectomy. At the time of laparotomy a deep infiltration of the uterine isthmus with infiltration of the bladder was found. Due to these findings radical hysterectomy was abandoned and the patient was treated with radiotherapy.

The third subject had stage IIB disease diagnosed at the 9th week of gestation. Clinical examination revealed a bulky tumor of the cervix with proximal parametrial involvement. On MRI examination a tumor with thinning of the stromal ring, suggesting left parametrial invasion

was detected. This patient was treated from eleventh week of gestation with radiotherapy consisting of external beam and intracavitary irradiation.

The fourth patient had a stage IA1 tumor (with focal invasion up to 2 mm) diagnosed in the 16th week of pregnancy. MRI confirmed the existence of a relatively small primary tumor of the cervix measuring 4x6 mm without infiltration of stromal ring. Basing on clinical, microscopic and radiological findings a decision was made to continue pregnancy. A repeated biopsy of the cervix and MRI on 32nd week of gestation confirmed stable disease with no sign of progression. The patient delivered by caesarean section in the 38th week of gestation and 6 weeks later amputation of the cervix was performed. Microscopic examination of the surgical specimen confirmed the presence of the tumor measuring 6x4 mm with the depth of stromal invasion of less than 2 mm.

Table I summarizes the main characteristics of the patients and their outcomes.

Discussion

The diagnosis of invasive cervical cancer in pregnancy is an uncommon clinical situation which poses a difficult situation both for the woman and her doctor. When detected in the first trimester, cervical cancer can be treated either by radical surgery or radiotherapy. Both methods of treatment may result in termination of pregnancy with ultimate loss of procreation potential. Diagnosis during the second trimester poses the most difficult clinical challenges. The decision whether to initiate treatment immediately or delay the treatment until foetus maturity should be based on the most precise data concerning the extent of the disease. Continuation of pregnancy without treatment could hardly be suggested to patients with parametrial infiltration or lymph node metastases. Staging based purely on clinical examination is not a reliable source of important prognostic factors, due to hyperaemia and oedema of the pelvic tissues associated with pregnancy [6-8]. Modern imaging techniques, such as ultrasonography have proven not to be a reliable staging tool in patients with cervical cancer. Computed tomography with an inevitable exposure of

Table I. Clinical features of the patients

	1	2	3	4
Age	24	29	31	32
FIGO stage	IB	IA	IIB	IB
Gestation age (weeks)	6	11	9	8
Treatment	radical hysterectomy	trachelectomy puerperium	rth*	explorative surgery + rth*
Treatment delay (weeks)	0	25	0	0
Microscopic exam	18 mm	2 mm	-	-
Stromal invasion				
Stromal invasion MRI	15 mm	0 mm	25 mm	22 mm
Pelvic nodes microscope	N (-)	-	-	N (+)
Pelvic nodes MRI	N (-)	N (-)	N (+)	N (+)

* radiotherapy

the fetus to irradiation is contraindicated in the first trimester [9, 10]. The latest reports have shown that MRI provides the best conditions to accurately define the extension of the tumor [11, 12]. The relative safety of this imaging technique even in the first trimester of pregnancy renders MRI the optimal method of pre-treatment evaluation of pregnant women with invasive carcinoma of the cervix [10, 11].

Tumor volume and tumor dimensions, depth of invasion of the cervical stroma and parametrial involvement are important prognostic factors on which to base the therapeutic decision concerning the method and the timing of treatment. Most investigators have found very good correlations of MRI findings with the results of measurements of the surgical specimen [13, 14]. Our data has shown an excellent correlation of pre treatment measurements with postoperative data even in the case of early invasive cancer. Some authors indicate that MRI tends to overestimate tumor volume by 10-35% [10, 11]. This inconsistency can be attributed to the inability of MRI differentiation between tissue oedema and tumor invasion [10, 11]. In our experience MRI failed to detect an infiltration of the vesico-cervical septum found intraoperatively. The status of the pelvic lymph nodes is the most important prognostic factor affecting the survival of patients with carcinoma of the cervix. The detection of positive pelvic nodes in the pre-treatment evaluation of pregnant women is crucial for selecting the patients for immediate or delayed therapy. The application of ultrasound and CT scan for assessing pelvic lymph nodes has been proven to bear a significant error [11]. More recent reports have shown significantly better consistency of MRI findings with microscopic examination of the nodes dissected at the time of surgery, with its sensitivity reaching approximately 60% and specificity exceeding 80% [10]. A limited number of cases in this report precluded any conclusive analysis, however it is worth to emphasize the 100% specificity of MRI in detecting node negative patients. The detection of macroscopic lymph node metastases on MRI is a contraindication to planned delay of treatment. There is an individual report advocating the use of neoadjuvant chemotherapy in patients wishing to continue pregnancy even in the presence of unfavourable prognostic factors, such as gross cervical tumor, suspect pelvic nodes or highly malignant histopathology [12-14]. The authors of the report emphasize the fact that the decision to start chemotherapy in the course of pregnancy was undertaken in circumstances under which the patient had decided to continue pregnancy despite the presence of a highly malignant tumor.

Because of a relative rarity of carcinoma of the cervix associated with pregnancy there are some limitations to the final assessment of MRI value in this particular clinical situation. Our early experience remains in accordance with other reports, as it confirms the value of MRI in the management of cervical cancer in pregnancy through providing important prognostic

information on which the optimal therapeutic decision can be based.

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