The significance of Doppler flow in early detection of uterine sarcoma in older primigravida pregnancies

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Summary

During a four-year period we analyzed the significance, sensitivity and sensibility of myoma Doppler flow during pregnancy in relation to the course and outcome of the pregnancy and to later histopathological findings.

By following 36 older primigravidas with determined myomas, we observed the course of the pregnancies in all trimesters and analyzed myoma Doppler flow. In conditions where the resistance index showed the possibility of uterine sarcoma, the pregnancy was ended by surgery; not only was myomectomy performed but also complete uterine hysterectomy with the previous consent of the patient. Doppler flow was accepted as the authoritative parameter for non-invasive detection of a malignant process.

Considering the obstetrical findings, other patients were delivered vaginally or operatively, but after puerperium they were subjected to control examinations and myomectomy because Doppler flow findings did not show any indications of sarcoma.

By histopathological analysis, we received benign results in 31 cases, while in four cases where we decided on hysterectomy and surgical delivery, we received malignant results, i.e. leiomyosarcoma.

In four cases of performed hysterectomy immediately after cesarean section, the resistance index (RI) of revascularization within the myoma was in the range between RI 0.30 ± 0.02. Flows within the uterine artery were 0.54 ± 0.03.

Key words: Sarcoma; Doppler; Pregnancy; Hysterectomy.

Introduction

Uterine sarcomas are very rare cases of tumors with the greatest malignant potential of all uterine tumors, and they differ significantly from endometrial carcinoma by their specific course, propagation and prognosis. Uterine sarcomas make up 3-5% of all uterine tumors [5]. Homologous uterine sarcomas originate from endometrial glands or endometrial stroma (endometrial stromal sarcoma) or the muscular layer of the uterus (leiomyosarcoma). Other types of homologous sarcomas (angiosarcoma or lymphosarcoma) originate from other tissues that are normally found in the uterus - blood and lymph vessels. Heterologous uterine sarcomas are composed of cells that are normally not found in the uterus (rhabdomyosarcoma, liposarcoma, chondrosarcoma, and osteosarcoma).

The relative incidence of certain types of sarcomas varies with different authors, but recent studies have shown that the most common one is carcinosarcoma [1]. The annual incidence of uterine sarcomas in the world is between 0.5 and 3.3 cases in every 100,000 women. According to the Harlow analysis [1], between 1973 and 1981 in the USA, the incidence of sarcoma in relation to different types was: carcinosarcoma (the most common) with an incidence of 0.82/100,000 and leiomyosarcoma with an incidence of 0.64/100,000. The risk of sarcoma is smaller in women who have had babies and decreases with the number of deliveries.

The incidence of uterine sarcoma in combination with pregnancy is rare in older primigravidas, and the course of pregnancy becomes questionable in medical and ethical terms [1].

Table 1. — *Classification according to Ober.*

Homologous	Heterologous
Pure	
Endometrial stromal sarcoma	
(Endolymphatic stromal myosis)	Rhabdomyosarcoma
Leiomyosarcoma	Chondrosarcoma
Angiosarcoma	Osteosarcoma
Fibrosarcoma	Liposarcoma
Mixed	
Carcinosarcoma tumor	Mixed mesodermal (Muller)
Classification according to the GOG*	
Leiomyosarcoma	
Endometrial stromal sarcoma	
Mixed Muller tumor (carcinosarcoma)	
Mixed heterologous Muller tumor (mixed mesodermal sarcoma)	
Other uterine sarcomas	

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As risk factors for this group of uterine sarcomas appear, those characteristic of endometrial carcinoma are: diabetes mellitus, hypertension and increased body weight. As these tumors are rich in receptors for estrogen and progesterone, long-term hormone therapy also presents a risk factor, especially the administration of tamoxifen in breast cancer.

Usually, uterine sarcoma is diagnosed after menopause. Leiomyosarcoma appears in women between 40 and 50 years of age. One of the usual symptoms is pain. An enlarged uterus for a short period of time is often present after menopause, thus this sign should not be attributed to uterine myomas.

The greatest number of sarcomas are diagnosed in clinical Stage I (in more than 50% of cases) [8]. However, in

Revised manuscript accepted for publication February 1, 2004

more than one-third of these patients, postoperative findings point to advanced processes.

Leiomyosarcomas make up less than 25% of all uterine sarcomas; propagation is local with spread to the blood and lymph vessels. Distant metastasis can appear even in cases where lymph node biopsy of the small pelvis was negative. In the histological diagnosis of leiomyosarcoma, mitotic cell activity has a crucial role. Certain types of leiomyomas can show more expressed cellularity or bizarre mitotic figures, but are considered benign if the number of mitosis on 10 microscopic fields (HPF) is less than 5. Tumors with a mitotic count from 5 to 10/10 HPF are classified as tumors of unknown malignant potential, while tumors whose mitotic figures (MF) are more than 10/10 HPF are considered malignant. According to most researchers [1, 5, 10], five-year survival is strongly related to the degree of mitotic activity, thus in sarcomas with less than 5/10 HPF the five-year survival rate is 95-98%, in tumors with 5-10/10 HPF around 40% and in those with over 10 MF/10 HPF it is around 15-12%.

Uterine sarcomas are treated surgically with total abdominal hysterectomy and bilateral salpingo-oophorectomy, selective lymphadnectomy of the pelvic and paraaortal lymph glands and peritoneal lavage. Even though at initial diagnosis most tumors are identified as Stage I, in more than 50% of these patients a process spreading outside the uterus can be found intraoperatively. Depending on the surgical findings, radiotherapy or chemotherapy can be applied postoperatively. Distant metastasis, especially in the lungs, can be surgically removed in some cases. Recurrences are not rare; they have a bad prognosis and are treated by chemotherapy [1, 7, 8].

Although in practice the FIGO classification is often used for endometrial carcinoma, determining the stage of the disease according to this classification is not a decisive prognostic factor. Studies have shown that in leiomyosarcoma, the duration of survival was only influenced by tumor mitotic activity, while the outcome of carcinosarcoma was influenced by stage and the age of the patient when the tumor was diagnosed regardless of the histological structure of the sarcoma [11]. In the case of endometrial stromal sarcoma, the prognosis is influenced by the degree of histological malignancy [9].

Material and Methods

Over a four-year period we analyzed the significance, sensitivity and sensibility of myoma Doppler flow during pregnancy in relation to the course and outcome of pregnancy, and in relation to subsequent histopathological results.

We analyzed 36 older primigravidas in each trimester. Routine parameters of pregnancy were followed and Doppler flows within observed myoma and uterine artery flows were registered.

Besides observed myomas, there were no other significant changes except the need to maintain pregnancy. After delivery, we compared the results of Doppler flows and the histopathological picture of the myomas.

Tests were statistically processed by the t-test and Fisher analysis.

Results and discussion

During the period between 2000 and 2004 at the ward for high-risk pregnancies, 36 older primigravidas were monitored. Patients were professionals and had no sterility or infertility, i.e. pregnancies were put off because of personal reasons and marriage at an older age. Age ranged from 34 to 42.

All patients were familiar with the risk of contractions, the necessity of following the pregnancy to term, conduction of double and triple tests and prenatal diagnosis. The condition of the fetus and fetoplacental unit also had to be followed with routine laboratory analyses and intensive myoma screening.

Doppler flow

Family history was positive in 70% of the cases. Before the pregnancy, patients had had no hormonal therapy and personal history did not point to other organ imbalances.

Body mass index in 89% of the cases was in the range from 30.4 to 71.4 signifying a large number of overweight women.

Cycles were shorter before pregnancy in many cases, i.e. they ranged from 24 to 27 days in 95% of the cases, which can be related to a mild progesterone deficit or estrogen surplus in fatty tissue. However since we had not followed these patients before the pregnancy we did not direct analyses towards these results.

In the first trimester all patients were diagnosed with myomas:

40 to 45 mm in 28 cases (group A);
45 to 60 mm in two cases (group B);
60 to 70 mm in one case (group C).

The myomas were intramural and partially subserous with different Doppler flows.

In group A the resistance index of myomas did not point to malignancy, with an RI of 0.54 ± 0.08; in group B it was 0.35 ± 0.12, and in group C it was 0.30 ± 0.10.

Uterine artery flow

In group A the resistance index within myomas did not point to malignancy, with an RI of 0.70 ± 0.08; in group B it was 0.65 ± 0.12, and in group C it was 0.45 ± 0.10.

During the second trimester, we determined an increase in myoma size in two patients in group B and a decrease in resistance index.

Myomas increased from 20 to 25 mm in two patients in group A with a significant decrease in the resistance index, leading us to put them in the risk group.

The third trimester

The RI in group A in 26 patients was still between 0.54 and 0.60.

In group B, four patients had decreased RI (0.30 ± 0.10).

In group C, one patient had an RI under 0.28.

The third trimester by uterine artery Doppler flow.

The RI in group A was still between 0.68 and 0.70 in 26 patients.

In group B four patients had a decreasing RI (0.60 ± 0.10).

In group C one patient had a RI under 0.30.

In agreement with the patients, the pregnancy was ended by cesarean in five mothers who delivered healthy children with body weights from 3,000 to 3,450 g. Subsequently we performed hysterectomy, omenectomy and the removal of lymph glands in the obturatory and inguinal region.

pH analysis of the material

Of interest is that the patient in group C with the greatest malignant potential had a spontaneous delivery of twins weighing 3,100 and 3,000 g at term (38 weeks of gestation).

In group A myomas did not point to possible malignant alterations and deliveries were ended depending on the obstetric indications.

After puerperium from 40 days to three months patients were hospitalized again and myomectomy was performed. In two cases there were complications that patients were warned about before surgery and hysterectomy was performed.

pH analysis of the material

In the first group of women undergoing surgery where myoma Doppler flow indexes pointed to malignant alterations, the results showed uterine leiomyosarcoma; in one patient it was FIGO Stage III coinciding to the lowest RI (0.28), while in the other four hysterectomies it was FIGO Stage II.

In 31 cases undergoing surgery for only myomectomy there were no malignant histopathological findings.

Following myoma Doppler flow is questionable during pregnancy and so is evaluation of validity, considering the resistance index shows decreased flow in circulation of the small pelvis during pregnancy.

The significance of following myoma Doppler flow and the decrease in morbidity and mortality in relation to a timely diagnosis should be emphasized.

None of the patients with ultrasonographic suspicious malignant processes or group A patients with uterine myoma per magnum had uterus torsion. The literature data show complications that were not present in our study [5].

The clinical picture is that of an abdominal catastrophe with severe abdominal pain or shock, and may be confused with placenta abruptio. The patient has acute abdominal symptomatology and requires laparotomy. Distortion may be attempted in early pregnancy. Cesarean section followed by hysterectomy is often required near term.

There were no fetal deaths in our study, although the literature data show up to a 50% incidence rate [9, 11].

Among our patients there were no miscarriages, and because of the location of the myomas there was no incarceration or difficult exit of the uterus out of the small pelvis. Also, the myomas did not move towards the endometrium, which explains the fact that not one of the patients miscarriaged.

Increased temperature and complications related to prolonged bleeding during delivery did not occur. In the literature data, given parameters exist if the myomas are located on the lateral segment of the uterus and towards the inner side of the uterus.

Conclusion

Myoma Doppler flow is also necessary during pregnancy and should always be kept in mind by physicians. Today it is common to observe pregnancy in older primigravidas and the focus must be on the embryo, fetoplacental unit, the mother and term pregnancy. Moreover, it is necessary to follow myomas as separate entities, and stress the importance of Doppler flow for a timely diagnosis.

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