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КЛИНИКА, ДИАГНОСТИКА И ПРОФИЛАКТИКА ВЕНОЗНЫХ ТРОМБОЭМБОЛИЧЕСКИХ ОСЛОЖНЕНИЙ ВО ВРЕМЯ БЕРЕМЕННОСТИ

CANCER AND PREGNANCY

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Abstract: Cancer and Pregnancy is a challenging conflict of interests between the mother's disease and the wellbeing of the fetus. Cancer in pregnancy is not any longer a rarity, because that disease already occur at younger age. On the other hand pregnancies are shifted into higher age groups. The incidence of cancer during pregnancy has a frequency between 0.1 % and 0.02 %.

It affects reproductive behaviour too. It is not only a medical problem, it is a psychological and social problem too – to wait hopefully to a child, cancer is a dramatic threat of live for mothers and the fetus.

Key words: breast cancer, pregnancy, ovarian cancer, surgery, delivery.

There are two different types of time of cancer leading to different problems:

1. Cancer during pregnancy
2. Pregnancy after cancer
3. Pregnancy during treatment

To the first problem: Cancer during pregnancy. During pregnancy, the mother is often seen first time since long time before by a health care professional like medical doctor, nurse or midwife. Sometimes they will find a cancer, which is developing since years. The incidence of cancer in pregnancy range from 1:1000 to 1:100 000 (table 1).

Malignancy	Incidence (per number of gestations)
Malignant melanoma	1:1000-10.000
Breast carcinoma	1:3000-1:10.000
Carcinoma of the cervix	1:2000-10.000
Leukaemia	1:75.000-1:100.000
Ovarian carcinoma	1:10.000-1:100.000
Colon cancer	1:13.000

Table 1. The incidence of cancer in pregnancy range from 1:1000 to 1:100 000 (National Cancer Institute 2014).

The diagnosis of cancer is not so easy during pregnancy because of psychological barriers and the fear to harm the fetus, e.g. by radiologic procedures like chest X-ray or abdominal pelvic CT.

The detailed doses of different X-ray targeting the fetus you can found in Pentheroudakis G. et al 2006. 100 mGy is common know as a threshold dose for teratogenetic in the first trimester. More than 250 mGy in the II and III Trimester is associated with fetal growth retardation and/or mental retardation.

Biopsies should be taken with special caution of bleeding and should be done under antibiotic shielding.

Surgery. The most surgical procedures in pregnancy are safe if you observe safety instructions, like positioning of the patient, special anaesthetic agents and procedures, antibiotic protection and if necessary induction of lung maturation and suppressing uterine contractions.

Chemotherapy. Chemotherapy is possible but not in the first trimester because of teratogenecity (especially MTX and cyclophosplamid). The most cytoxic drugs can cross the placenta. Anthracyclines seems to be much safer. There is also no evidence of induction of tumours in the offsprings. Hormonal therapy is a contraindication in pregnancy. Biologicals or antibodies should not given in pregnancy too, because of little experience with these substances.

Breast cancer. The highest incidence of carcinoma during pregnancy in Europe is the breast carcinoma. Breast cancer associated with pregnancy is defined as diagnosed during and twelve months after delivery (PABC, Pregnancy associates Breast Cancer). The incidence of PABC is depended on mother's age: 0.002% to 0.23% (Haas et al.: Int. J Cancer 1994). The diagnosis of breast cancer in pregnancy or during breast feeding is delayed because of mastodynia and frequent nodes during breast feeding. And the delay in diagnosis leads to a higher stage and more involvement of lymphatic nodes.

Diagnosis. Mammography during pregnancy is possible by shielding the abdomen, but it is not so sensitive like in non-pregnant women, because of density of the breast. Ultrasound can be used during pregnancy without any

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risk. The diagnosis can be done by magnetic resonance imaging too. There is only a theoretical risk before gestational week 15. Gadolinum, used as a contrast substance should not be used during the first trimester too. From FDA it is classified as a group C medication. Most important for diagnosis is the palpation of the breast. At least once in the beginning of pregnancy. In Austria it is demanded by the state authorities before week 16th. The tumour is often found by the patient her selves. But often the symptoms are ignored and interpreted as normal and physiologic. If breast cancer is suspected, a needle biopsy has to be done. For the pathologist it is not easy to differentiate the tumour. The incidence of grade 3 (undifferentiated) is higher than in non-pregnant cancer.

Clinic. The standard procedures for monitoring the pregnancy and for cancer treatment should be done. The monitoring of pregnancy should be focused on fetal growth retardation and red and white blood count. Erythropoetin and GCSF can be used in pregnancy. Antiemetic drugs, like andrasetron or lorazepam are allowed.

Delivery. Monitoring of pregnancy. Mother and fetus can be monitored with prenatal standard care before starting chemotherapy ultrasound of the fetus must be performed. Evaluation for fetal growth should be performed before every cycle of chemotherapy. In case of abnormal findings more stringent monitoring of the fetus or even preterm delivery might be necessary.

Pregnancy-related complications such as preeclampsia and preterm labour should be treated based on standard recommendations.

Timing of delivery. Labour can be induced or cesarean section performed when the maturation of the fetus is sufficient. Timing of delivery can be optimized in relation to the treatment of breast cancer. If chemotherapy is planed to continue after delivery, vaginal delivery may be less likely because it delays the initiation of chemotherapy. Patient's personal preferences and previous obstetric history should be considered. Delivery should occur approx 3 weeks after the last dose of antrazycline-based chemotherapy (no CHT after 35 week, because of the risk of spontaneous delivery in the neutropenic period). If preterm delivery is inevitable, fetal lung maturity is essential. Termination of pregnancy does not improve maternal outcome.

If further systemic therapy is needed after delivery, breast feeding may be contraindicated depending on drug toxicities.

Surgery. Surgery is safe during at any stage of pregnancy. But before the 12th week it can be complicated by abortion. Every kind of breast surgery e. g. breast conserving surgery is possible. Left lateral position is necessary. Keep in mind that thromboprophylaxis with low molecular weight heparin has to be done for longer time.

The role of the sentinel node biopsy in early stage breast cancer in pregnancy has not been evaluateted sufficiently. There is also the possibility that perhaps the lymphatic passway has altered in the pregnant breast. Lamphyzurin used for identification of the sentinel lymph node is a category C drug and should not be used in pregnancy. Recent studies claims radiocoloid agents such as technic-99m, has low radioactivity and should not be considered as a contraindication, but it should be only used in scientific randomized studies.

Systemic chemotherapy may be necessary for the treatment. The benefits for the mother must be compaired with the potential longterm harm to the fetus from inutero exposal to chemotherapy agents.

The overall risk for congenital malformation is reported with 2-3%. The incidence of major congenital malformations after using cytotoxic drugs is also about 3%, but in the first trimester it range from 10-20%. The risk of malformation decreases in the second and third trimester to 1.3%.

The long term implications for the child can show that there is low adverse impact on development in the children exposed to antracycline based chemotherapy in utero. [1,6].

A large study with median follow-up of 18.7 years of 84 children: there is no evidence of physical congenital abnormalities or any neurologic psychological abnormalities. Children demonstrating normal learning and educational behaviour.

The German Society for Senology has established a register for breast cancer and pregnancy [3].

Cervical cancer. The management of preinvasive cervical disease means that diagnostic procedures should be the same like in non-pregnant women.

In case of abnormal cytological findings a colposcopy with a biopsy has to be done, but it has only a sensitivity of 73-95%. The cervical curettage should not be done! If there is no invasion, treatment during pregnancy is not necessary. Waiting till the post partal period is possible and recommended.

If there is a microinvasion in early pregnancy a large loop-excision should be done immediately.

In case of invasive cancer there is an ethical conflict between the best management of cancer and induction of abortion. The procedure should be discussed with the parents and oncologists, obstetricians, pathologists and perinatologists.

The management of invasive cervical cancer depends on the stage of pregnancy, too. In the first trimester a lymph node dissection by laparoscopic procedures are possible. Perhaps in combination of trachelectomy. In the second and third trimester is given, caesarean section combined with radical hysterectomy, neoadjuvant

chemotherapy shoud be offered at the earliest time, after lung maturation.

The prognosis of cervical cancer in pregnancy does not differ to non-pregnant women, if compared to the stage and lymphotic node involvement [7].

Ovarian Cancer. For best is ultrasound in combination with coloured Doppler or MRI could be used. Tumour markers (CA 125) are elevated in normal pregnancies, too. Tumour mass should be removed at every time in pregnancy. After the 18th week a chemotherapy should be offered.

Before week 12th additional therapy with progesterone should be done.

For all types of cancer in pregnancy is mandatory to provide psychological help [2].

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РАК И БЕРЕМЕННОСТЬ

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Резюме: рак и беременность представляют собой серьезный конфликт интересов между заболеванием матери и благополучием плода. Рак при беременности в последнее время перестал быть редким явлением, поскольку болезнь теперь развивается и в более раннем возрасте. С другой стороны, беременность часто откладывается до более позднего возраста. Частота онкологических заболеваний во время беременности составляет от 0,1 до 0,02%. Проблема затрагивает и репродуктивные поведенческие аспекты. Это не только медицинская проблема, но также психологическая и социальная – очень трудно с надеждой ожидать появления на свет ребенка, когда рак представляет смертельную угрозу жизни матери и ребенка.

Ключевые слова: рак молочной железы, беременность, рак яичников, хирургия, роды.