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BREAST CANCER IN PREGNANCY - CASE REPORT

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ABSTRACT

Breast cancer in pregnancy (BCP) is relatively rare with an incidence of 1:3000 to 1:10 000 births. Breast cancer in pregnancy is second most frequent among malignancies in pregnancy, right behind cervical cancer. The diagnose of BCP is made if the condition appears during the pregnancy, or during the first year after delivery, with some variations in the duration of the postpartal period that is taken into concideratrion, varying from 6 months to 2 years. Most of the tumors are adenocarcinomas, scirus, colloid or anaplastic. As in all cases of breast cancer outside pregnancy, biopsy is a "gold standard" in the diagnosis of this condition during pregnancy. Immaging diagnostic techniques have limited aplication either because of the increased faulse positive rate or lower sensitivity. Pregnancy termination does not represent an efficiant terapeutic alternative. Surgical treatment is a supreme therapeutic procedure in the treatment of BCP. In patients that have been diagnosed during the late second trimester, optimal treatment comprises of disection of the tumor mass and axillar lymph nodes, followed by delivery and radiation therapy.

We are presenting a case of 34 years old patient with poorly differentiated invasive breast carcinoma, Stage IIIC, during the late second trimester. After the surgeri the delivery was postponed until the 37th week. Through presentation of this case we've tried to show, that there is an open posibility to postpone the delivery in patients in which the diagnosis was made in the late second trimester for until the late third trimester or even until the EDD, and yet not to compromise overall prognosis for the patient.

Key words: Breast cancer, pregnancy, biopsy, delivery, radiation therapy.

INTRODUCTION

Diagnosis of breast cancer in pregnancy (BCP) is relatively rare. The incidence of this entity ranges within the limits of 1:3000 to 1:10 000 births (1), with an increasing rate, wich can be explaned by the fact that increasing number of women by choise or by circumstance are becoming pregnant later during their reproductive period. According to the statistical data, breast cancer in pregnancy is second most frequent among malignancies in pregnancy, right behind cervical cancer (2,3,24).

In most of the cases, breast cancer in pregnancy is presented as a painless palpable mass in the gland tissue, associated with niple disscarge that emerges form time to time. However, one should have in mind that in almost 80 % of the cases, manifested changes are of benign nature (4).

Most of the authors think that the diagnose of BCP is made if the condition appears during the pregnancy, or during the first year after delivery, with some variations in the duration of the postpartal period that is taken into concideratrion, varying from 6 months to 2 years (5,6).

If you consider the histological changes in the brest tissue that appear during pregnancy by the influence of the pregnancy hormones, and if we take into account that the overall mass of the brests is doubled, than it becomes very clear that making a diagnose in these patients is quite difficult. Hence, the diagnose is delayed for 1-2 months comparing to the non pregnant women. On the other hand, breast cancer can grow rapidly during pregnancy, and metastases in the regional lymph nodes can appear very early. It is yet not clear, whether it is a consequence of the delaying the diagnose, increased vascularisation. hormonal influence or immunosuppression activated during pregnancy. According to the results of some studies, possibility for presence of distant metastases by the time the diagnose is made, is 2.5 times higher. In 56 83% of these women byd not b the time the diagnose is made, affected lymph nodes can be found. (2,6-11)

Most of the tumors are adenocarcinomas, scirus, colloid or anaplastic (75-90% are ductal carcionmas). In the

differential diagnosis gular turble, restit disease lobular so that the pathologist can take into consideration the invernissia, linunass, isamartunass and fibrocystic disease cer beconsidered Awardinumes, say comes and neurinomes are rearly sear, but should not be discaveled, and the same gues for the time milesis of the breast (9.10).

MARCHINE THE DIAGNASSE

Different imaging techniques can be used in order to diagrasse BCP, but attention should be paied to their sensitivity in pregnant women. Negative influence to the ienssimi dische mucderet when using this techniques.

Maninography during pregnancy is associated with nuressed care of faulse positive findings due to the changes, increased tensity of the gland tissue. This means that there is a limitation of the use of this method in prepart women. However, mammography is considered safe furing pregnancy, since the maximal exposure of the fetus in standard two directional mammography is 0.4 ment (LOH4 Gov 102 15 14)

Ultresound is cheap and can be used as a first line diagnostic procedure. It provides possibility for differentiation between solid and cystic masses in up to Fig of cases 15).

MRI in non pregnanat women is highly sensitive but with limited specificity. During pregnancy, the use of MRI is considered to be related with two possible riscs to the ferus: cavitations and thermal effects. It should be kept n mind that Gadolinium crosses placental barrier and can be associated with fetal anomalies which puts it in tie C class (substances and medications which can be used only if the benefit outweighed the potential risks). 14.16.17 The use of MHI outweighes the use of ultrasound in deteliting liver metastases, and the same goes for other maging techniques in detecting brain metastases (14).

Radiography of the lungs, in two standard directions, lateral and autero-posterior, is considered to be safe, since the maximal exposure of the fetus is 0+0,01 rad (0+0,0001 Gv) (14,18).

As in all cases of breast cancer outside pregnancy, biopsy is a "gold standard" in the diagnosis of this condition turing pregnancy. So called "core needle" biopsy is a method of choise, but fine-needle aspiration biopsy can also be used. In order to prevent complications such as fictiation of haemathomas, it is recommended that the Procedure should be performed after previous of the breast, especially in lactating women. When sending the Material for histology, it is mandatory to note that the dissue sample comes from a pregnant or lactating woman,

appearing physiological hyper proliferation (19-23).

TREATMENT

Pregnancy termination does not represent an efficient terapeutic alternative. Up until now experience and data from studies have shown that overall prognosis doesn't improve with termination of pregnancy and by applying standard therapeutic protocols. Even in cases with advanced disease, terminating pregnancy and performing bilateral cophorectomy for reduction of hormonal stimulation of the malignant tissue, didn't produced expected improvement in the survival rate (25,26,27).

Surgical treatment is a supreme therapeutic procedure in the treatment of BCP. Risks associated with this therapeutic modality include possibility for miscarriage and preterm delivery. Approximately 0.5-2% of all pregnant women are submitted to invasive procedures during pregnancy, starting with biopsy ending with major surgical procedures (28).

Breast surgery is considered to be relatively safe during pregnancy. Mastectomy in combination with armpit lymph nodes dissection is an optimal surgical solution in patients with stage I and II of the disease, as well as in patients with advanced stage disease (Stage III) that want to continue their pregnancy. Mastectomy eliminates the necessity for radiation treatment in early stage disease, considering the existing risk to the fetus. On the other hand, dissection of the axillar lymph nodes, provides a possibility for determination of the nodal status which is very important in making decision for the postoperative chemotherapeutic protocol (14,29).

In patients that have been diagnosed during the late second trimester, optima treatment comprises of disection of the tumor mass and axillar lymph nodes, followed by delivery and radiation therapy. If the diagnose is made early in pregnancy it is opcional to perform so called breast-conserving surgery, and than, after the first trimester is over to apply chemotherapy, followe by radiotherapy in the postpartal period (30,31,34).

According to the individual approach, it is posible to deliver the baby by elective C-Section, when appropriate fetal maturation, mostly reffering to fetal lungs matiration, is achieved.

Radiation therapy, by defualt, is not applied during pregnancy since it represents a significant risk to the fetus: first, because of the posible teratogenic effect, including

the possibility for development of fetal malignant tumors and blood malignancies in the newborn, and than because of the toxic effect of the radiation which depends on the stage of fetal development, applied dose, intensity and distribution of the radiation.

Posibility for fetal loss is at its highest point during the preimplantation period (0-9 days after conception), and radiation induced malformation appear if the exposure takes place during the period of organogenesis (15-50 days after conception). Intrauterine grouth restriction, mental dissability and radiation induced carcinogenesis appear in corelation with radiation exposure during the first trimester.

If stantdard radiation therapy protocols of 5 000 rad (50 Gy) are applied, the dose of fetal exposure goes from 3,9 – 15 rad (0.039-0.15 Gy) during the first trimester, up to 200 rad (2 Gy) by the end of the pregnancy, when the growing uterus gets closer to the diaphragm. In any case these doses of fetal exposition are higher than those concidered to be safe (0.05 Gy) (32,33,35).

As far as chemotherapy is concerned, all of the chemotherapeutic agents are classified as Class D, according to the US FDA regulations for safe medications in pregnancy, which practicaly means that they belong to a group of drugs that are concidered to be dangerous and with teratogenic effect. Still, if the period of organogenesis is passed over, large number of studies, up until now, have show rather high safety profile if used during pregnancy (36-40). Most frequent complications associated with the use of chemotherapeutic agents during pregnancy are: preterm delivery, intrauterine growth restriction, low birth weight, transitury apnea and transitory leukemia of the newbon. Long term effects of the chemotherapeutic agents to the offspring are not well defined yet (37,40-42). Standard therapeutic protocols for treatment of BCP include Doxorubicin, Cyclophosphamide and Fluorouracil. Defining the dose of the agents during pregnancy is aditionaly complicated by the increase of the plasma volumen, kidney-liver function, decrease of the plasma concentration of the albumen fraction and reduction of the gastric secretion, as well as with the possible influence of the amniotic space as an additional comaprtment(36,44).

PROGNOSIS

Prognosis of the BCP has changed radically compared with the early beginnings and first published cases. Today,

it is considered that the final outcome is as same as in the non pregnant population, modified according to ${\rm age}$ and stage of the disease. The rate of five year survival is 57-82% in pregnant women compared to 56-82% in $_{\mbox{\scriptsize non}}$ pregnant women. Minimal differences appear when lymph nodes status is discussed (47% of pregnant women and 59% of non pregnantwomen are found to have positive lymph nodes)(2,9-11,15,45-47). The question of pregnancy following previous pregnancy complicated by BCP stays still unanswered, because there are no data from relevant studies that can put some light on the subject. Data from limited number of cases which were published up untill now, suggest that the pause between the pregnancy complicated by BC and following pregnancy should not be shorter than 2 years. Some oncologists recommend that the pause should be at least 5 years in patients who have had stage III disease, and do not recommend getting pregnant ever in patients with stage IV disease. (6.48-50)

Anyway, decision sholud be based on the posible wors case scenarion in case of reappearence of the disease during or after the following pregnancy.

CASE REPORT

Our patient is a 34 years old G3 P2 Ab0.

During the eigth month of her pregnancy (28-32 w.g) she has noticed a presence of a lump in her right brest, and after consulting her family physician, she was referred to a radiologist. Ultrasound of the brest was done, and the finding was as follows: In the lower lateral quadrant of the brest, large heterogenous formation with iregular shape is present, 4x2.5 cm in diametter. No changes in the ipsilateral axilla were detected. The contralateal, left breast appeared nomal on US. Because of the actual pregnancy, mammography was not performed.

After the ultrasound examination, fine needle aspiration biopsy was performed. Hystopathological analysis of the tissue semple confrmed the suspition of malignancy. Large number of single cells and cell groups were seen in the tissue semple with distigushed caracteristics of malignancy (Cytology gruop V).

After the hystologyc verification, patient was admitted at the university clinic for obstetrics and gynecology in Skopje, with primry intention for the pregnancy to be terminated by giving birth, so that surgery on the primary process can be performed, by recomendation of the surrgeon. The patient was in her 34th week of pregnancy. Detailed evaluation of the pregnancy was done. Since there

was no obstetrical indication for delivery, consultation with cardio-thoracic surgeon was made, the decision for delivery was postponed and the patient was refered to the university clinic for cardio-thoracic surgery in Skopje. The ide a was to make a mastectomy with axillar lymph node dissection, and after the surgery to evaluate the condition of the pregnancy and to postpone the delivery for as far as posible to the estimated date of delivery. Aditional oncologycal treatment of the carcinoma was planed for after the delivery.

Following adequate preoperative preparation operative intervention was performend. Radical mastectomy, Madden modification has been performed at the University clinic for thoraco-vascular surgery in Skopje. No intraoperative nor postoperative compplications were registred. Patient was released at the third postoperative day with good general condition. Tissue material that was extirpated during operation comprised of mammary tissue of the right breast with overlying skin, 13x7 cm in diameter, fibrous and fatty tissue 4 cm high and muscle tissue with dimensions 10 x 6 x 2.5 cm attached to it. Tissue sample from the right armpit comprised of fatty tissue with dimensions 9 x 4 x 3.5 cm, containing 14 lymph nodes, 2 x 0.4 cm. Dissection of the mammary glandular tissue showed a presnce of a gray tumor mass in the lateral quadrants 4.5 x 4.3 x 3 cm. With microscopical analysis, this tumor tissue presented as a poorly differentiated invasive breast carcinoma, whereas the microscopical evaluation of the lymhoglandular tissue of the right axilla showed a presence of metastases in all of the 14 lymph modes one of which had a pennetration through the capsule. According to this finding the disease was in Stage IIIC, and the deffinitive postoperative clasiffication was declared as it follows: pTNM = pT2 pN3 pMx G3 C4, Stage IIIC.

Followint the opperation the patient was admitted at the University clinic for obstertics and gynecology in Skopje. According to the data on last menstrual period (LMP) the pregnancy was in its 36th week of geastation. Ultrasound examination was performed. A singelton pregnancy was confirmed. Fetal biometry results were as follows: BPD=101 mm, AC=326 mm, FL=73 mm, HL = 62 mm, placenta lieing on the posterior uterine wall. The fetus was in vertex presentation. After 7 days spontaneus contractions were established and the patient gave birth to a healty baby boy weighing 3450 gr and 50 cm in length. Apgar score, 8 following 1' and 9 in 5'. 48 hours after the delivery, the mother ant the child were released from

the hospital. The mother was advised to take ablactation therapy (Bromocriptine 1.25 mg / 12h).

Two weeks after the delivery ultrasound of the abdomen and radiography of the chest and the spine were performed. No evidence of metastatic deposition in the liver, lung or spine were found.

By the period when this report was finished, the patient was in good general condition with no sings of recurence of the primay illnes.

DISCUSION

As mentioned erlier in this paper, supreme therapeutical option for BCP is surgery, consisting of radical mastectomy with lymphadenectomy in the ipsilateral axilla. (14,28,29) Most of the autors reccomend postponing the delivery after the surgery until fetal lung maturation is achieved, espetially in patients in which the diagnosis is made in the late second trimester. However, there is no general standing on the appropriate gestational age for delivery once maturity is reached. Never the less, in most of the cases delivery is acomplished right after maturation in order to provide conditions for begining of the radiotherapy and chemotherapy as sson as posible.

Through presentation of this case we've tried to show, that there is an open posibility to postpone the delivery in patients in which the diagnosis was made in the late second trimester for until the late third trimester or even until the EDD, and yet not to compromise overall prognosis for the patient. Wheter there is a posibility for postponing the delivery util spontaneus onset of contractions, as in our patient, or actions of induction of labour should be undertaken EDD is aproaching, is still to be debated. However, in our opinion, this posibility shoud not be dissmissed, espetialy when the patient is a multiparous.

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КАРЦИНОМ НА ДОЈКА ВО ТЕК НА БРЕМЕНОСТ - ПРИКАЗ НА СЛУЧАЈ

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АБСТРАКТ

Карциномот на дојка во тек на бременост е релативно редок, со инциденца од 1:3000 до 1: 10 000 породувања. По својата фреквенција се наоѓа на второто место помеѓу малигните заболувања во текот на бременоста, веднаш зад цервикалниот карцином. Дијагнозата на заболувањето се поставува доколку истото се манифестира во текот на бременоста или во текот на првата година по породувањето, со варијации кои се однесуваат на постпарталниот период во итервал од 6 месеци до 2 години. Најголемиот број од карциномите се аденокарциноми, скирозни, колоидни или анапластични. Како и во случаите на мамарен карцином кај небремените жени, така и овде, "златен стандард" во дијагнозата претставува тенко иглената биопсија. Визуелизациските дијагностички методи имаат ограничена апликативна вредност како заради ниската сензитивност, така и заради зголемувањето на стапката на лажно позитивни резултати. Прекинот на бременоста не представува ефикасна тераписка алтернатива. Хируршкиот третман представува императив во лекувањето. Кај пациентките, кај кои дијагнозата е поставена во текот на доцниот втор триместар од бременоста, оптималниот тераписки пристап го сочинуваат дисекција на туморската маса и аксиларните лимфни јазли, на што ќе се надоврзе породување и радиотерапија.

Овој приказ на случај опишува 34 годишна пациентка со лошо диференциран инвазивен мамарен карцином, Стадиум IIIC, дијагностициран во доцниот втор триместар. По спроведената хируршка итервенција, породувањето беше одложено до 37-та гестациска недела. Со презентацијата на овој случај, се обидовме да покажеме дека постои отворена можност за одложување на породувањето кај оваа група на пациенти до доцниот трет триместар па дури и до веројатниот термин за породување, без при тоа да се загрози прогнозата и позитивниот исход кај пациентката.

Клучни зборови: Карциномот на дојка, бременост, тенко иглената биопсија, породување , радиотералија.