Case report

UNRECOGNIZED PREGNANCY AND CHEMOTHERAPY

Dragan Loncar

Teratogenic potential of cytostatics is directly dependent on pregnancy stage in which they are applied. Without any doubt, teratogenic potential was proved to be the highest in the 1st pregnancy trimester, especially during treatment by polychemotherapy, in the range of 10% to 16%, 3% of which goes to large anomalies which attack fetus. The effects related to fetus depend on pregnancy stage, dose quantity and synergism with other medications, as well as on individual reactions to the medication. The role of placental »barrier« causes certain doubts. In the 2nd and 3rd trimester the application of these medications can be the reason of setback in the development in utero, premature birth and neurotoxicity. The area of chemotherapy application in the 2nd pregnancy trimester is definitely the most controversial, because at that moment the termination of pregnancy represents enormous psychological and ethical burden both for the parents and the doctor. If the decision is made to continue the therapy by cytostatics, it can be applied with obligatory informing of parents on potential risks for the fetus. In the 3rd trimester, however, it seems that it is acceptable to postpone the application of cytostatics till after the child is born. The aim of this paper was to present the case of unrecognized pregnancy of the woman in the 24th gestation week after the operation due to colon carcinoma, with verified metastases in the liver and ongoing chemotherapy, whose pregnancy was established accidentally after detection of the skeleton at control native x-ray screening of abdomen in the Clinical Centre Kragujevac. *Acta Medica Medianae 2009;48(1):63-65.*

***Key words**: colon carcinoma, chemotherapy, pregnancy*

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Case report

The patient, M. Z. (40 years old), a housewife, was sent to CGO CC Kragujevac because of the abortion of unrecognized pregnancy in the later stage because of the active malignant disease with metastatic changes on the liver and completed chemotherapy which was incidentally discovered by the Roentgen diagnostics on the X-ray control screening of the fetal skeleton.

Chemotherapy was put into effect during the period of the early organogenesis of the fetus in the official oncology centre according to the procedure suggested by the medical consultation.

The patient was admitted in the CGO CC Kragujevac with the following diagnosis:

Graviditas ml VI. St post op pp Ca colonis et CHT, Meta in hepate, St post metastasectomiam, Progresio morbi, CHT paliativa in coursu.

Per anamnesis:

- the patient had been operated a few times because of the basic disease and treated with cytostatics
- she did not know the exact date of the last menstrual cycle
- two deliveries, two children.

Ultrasonographic examination

The pelvis surpasses, BPD 55 mm, HC2 216 mm, AC 163 mm, FL 42 mm, amniotic fluid normal, the activity of the fetus's heart detected, placenta on the front wall homogenous, NG at UZ HBd 23,1.

Laboratory analyses

Le $12x10^9$/l; Hgb 98 g/l; Plt $204x10^9$/l fibrinogen 6,34 g/l; aPTT25,0s; INR 10,0s; FVIII 201; FIX 115; FII 115%.

Blood type of the patient: A RhD+

Biochemistry

AST 18 U/l; ALT 19 U/l; LDH 745 U/l; glc 4,3 mmol/l; urea 2,0 mmol/l; creatine 53 mmol/l; albumin 34 g/l.

The case of the patient was presented to the Ethical Committee CC Kragujevac and they agreed that the abortion of the pregnancy was necessary due to the medical indications.

Before the procedures of the miscarriage induction and feticide were completed, the consultative, transfusional support had been ensured concerning the parameters of coagulating status of the patient.

At the Department for the Fertility Control, the feticide was carried out by the procedure of cardiocentesis applying 5 ml 7,4% KCl, and by the

miscarriage induction with intraamnial application 400 ml 20% natrii chloride infundibule, under the control of the ultrasound.

Discussion

In general population of women capable of reproduction, some 3-5% of them have a risk to give birth to a child with various deffects. The use of chemotherapy significantly increases that risk. The combination of this therapy with surgical and radiologic treatment significantly improved the possibility of recovery of the patients suffering from malignant diseases (5). Simultaneously, the risk of giving births to malformed fetuses is increased in the current pregnancy as well as in all future pregnancies. The cause of these occurrences is in non-selective effect of these medications on the growth and development of embryo's and/or fetus's cells during the course of the current pregnancy as well as in non-selective influence over the cells of the reproductive system of a patient. The influence of chemotherapy over the genome is unpredictable from the quantitative and qualitative point of view. The negative effect can be seen in the domain of the immunological status of a treated person (6). You are not supposed to predict any prognosis concerning the period of time necessary to establish homeostasis again in patients taking chemotherapy. Repairing mechanisms do not possess any unlimited possibilities and they are individually dependant. We can find a very small number of reports in literature that deal with this problem. Without hesitation, the greatest teratogenesis was proven in the first trimester of pregnancy, especially with the use of polychemotherapy in the range between 10% and 16% from which about 3% concern great anomalies of a fetus.

The effects concerning the fetus depend on the stage of the pregnancy, dose quantities and synergism with other medications as well as with individual reactions to medications. Confusion is caused by the role of placenta ''barrier". Whereas it can be a strong bioloical barrier for some antineoplastic medicine, most of them, however, penetrate it with the direct influence over the embryo. During the second and third trimester the use of these medications can be the reason for a slowdown in the development in utero, as well as for the prematurely born children and neurotoxication. It is certainly the most controversial domain of the use of chemotherapy in the second trimester of pregnancy, because the abortion of the pregnancy at that stage is an extremely psychological and ethical burden for parents and a physician. If you make a decision to continue using the cytostatic therapy, it can be used with the obligatory informing of the parents about the potential risks for the fetus. In the third trimester it seems that it is acceptable to postpone the application of cytostatics until the post natal period.

Medicines are classified in different ways according to their harmful influence over fetus. Chemoterapeutics are, unfortunately, the group of medicines which, without an exception, belong to so-called ''D" group which includes remedies from which you can expect the increased frequency of malformations or irreversible damages of fetus, and there aren't any unharmful cytostatics for the fetus in pregnacy (8). Chemotherapy is contraindicated during the period of breast feeding because cytostatics go to mother's milk, and that is why you should stop breast feeding because of the influence over the immunological system of a child. According to the data from literature, it is necessary to delay pregnancy for several months after the previous use of chemotherapy because of the above mentioned influence over the reproductive cells. (9) Fathers-to-be are advised, if they need the use of chemotherapy, to deposit sperm before the treatment (10). Each pregnancy which is actualized after the use of chemotherapy must be considered too risky and it is necessary to follow it as a pregnancy of high risk, including the fetus as well as the mother.

Conclusion

Pregnacy is not at all recommended during chemotherapy. Luckily, cancer is very rare among young women capable of giving birth. When chemotherapy is used you must take care not only of the mother but also of the fetus which is supposed to develop in such circumstances. Cytostatics have double effect. First, they directly damage the fetus, and thus, by damaging egg cells, later pregnancies may result in giving birth to children with genetic anomalies. Therefore, when you start chemotherapy, the pregnancy that already exists in the first trimester should be ended if the chemotherapy is necessary for mother's survival. Thus, you should strictly take care that a woman doesn't get pregnant during chemotherapy or at least six months after its use. Later, in the case of pregnancy, one should carry out the genetical examination using the methods of prenatal screening.

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NEPREPOZNATA TRUDNOĆA I HEMIOTERAPIJA

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Teratogenost citostatika direktno je zavisna od stadijuma trudnoće u kojem se koriste. Bez ikakve nedoumice, najveća teratogenost dokazana je u I tromesečju trudnoće, posebno pri primeni polihemioterapije i to u rasponu od 10% do 16%, od čega oko 3% otpada na velike anomalije koje zahvate fetus. U II i III tromesečju primena ovih lekova može biti razlog zastoja u razvoju in utero, zatim nedonešenosti i neurotoksičnosti. Svakako je najkontroverznije područje primene hemioterapije u II trimestru trudnoće, jer tada prekid trudnoće predstavlja izuzetno psihološko i etičko opterećenje za roditelje i lekara. Ukoliko se donese odluka za nastavak terapije citostaticima, ona se može primeniti uz obavezno informisanje roditelja o potencijalnim rizicima za fetus. U III trimestru, čini se, ipak, da je prihvatljivo odložiti aplikaciju citostatika do posle porođaja. Cilj rada bio je prikazati slučaj neprepoznate trudnoće u 24. gestacijskoj nedelji kod žene nakon operacije zbog karcinoma kolona, sa verifikovanim metastazama u jetri, hemioterapijom u toku, kod koje je trudnoća slučajno otkrivena nakon prikaza skeleta pri kontrolnom nativnom Rentgen snimanju abdomena u KC Kragujevac. Trudnoća se za vreme hemioterapije nikako ne preporučuje. Srećom, rak se znatno ređe javlja kod mladih žena sposobnih za rađanje. Kod primene hemioterapije mora se voditi računa ne samo o budućoj majci nego i o plodu koji treba da se razvije pod takvim okolnostima. Citostatici deluju dvostruko. Prvo, direktno oštećuju plod, a zatim, oštećujući jajne ćelije, kod neke kasnije trudnoće mogu dovesti do rađanja dece sa genetskim anomalijama. Zato, kod otpočinjanja hemioterapije, već prisutnu trudnoću u prvom trimestru treba okončati, ako je hemioterapija neophodna za preživljavanje majke. Prema tome, trebalo bi strogo voditi računa da žena ne zatrudni u toku hemioterapije i bar još šest meseci nakon njenog sprovođenja. I kasnije, u slučaju trudnoće, trebalo bi sprovesti genetsko ispitivanje plodove vode kao i druge metode. *Acta Medica Medianae 2009;48(1):63-65.*

***Ključne reči**: karcinom kolona, hemioterapija, trudnoća*