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Case Report

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Case of pregnancy favorable outcome in a patient receiving hemodialysis therapy

Abstract

Pregnancy is the most important period in woman's life. The health of a mother and a baby depend on how comfortable and safe this period goes. However, pregnancy in patients with the end-stage chronic renal failure (ESCRF) receiving renal replacement therapy (RRT) by program hemodialysis (PHD) is associated with a high risk of complications at all stages of pregnancy development. A comprehensive approach to the treatment of such patients involves the interaction of Obstetricians and Gynecologists with Dialysis Department experts, adequate dialysis therapy in combination with pregnancy prolongation measures. This article represents a case of a successful pregnancy resolution in a patient receiving PHD lasting more than 22 years. We have explored the actual issues of dialysis therapy correction. We have described the problems of the woman's body preliminary six-month training, monitoring of the early diagnostics of pregnancy and further antenatal and obstetric care in critical situations by Caesarean section in 27-28 weeks pregnancy with a live male fetus.

Keywords: pregnancy, chronic program hemodialysis, end stage of chronic kidney failure

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Abbreviations: ESCRF, end-stage chronic renal failure; RRT, renal replacement therapy; PHD, program hemodialysis; HCG, human chorionic gonadotropin; MBD, mineral and bone disorders; URR, urea reduction ratio; PCL, parietal-coccygeal length; NT, nuchal translucency; EPO, epoetin-alfa; PCD, protein-calorie deficiency; EMA, emergency medical aid; CC, cervical canal; CKD, chronic kidney disease

Introduction

Motherhood is neither more nor less than the state of the female body determined by child-bearing, child birth and breastfeeding, involving her into a new quality of existence. Medical supervision is important at every step, from diagnosis of pregnancy to delivery. It is known that early detection of pregnancy in patients with ESCRF treated with PHD is difficult, due to the initial increase in serum beta-chorionic human gonadotropin.[1–3] The average frequency of conception in women of childbearing age is low and is in the range from 0.3% to 1.5% a year.[3] At the same time, despite a high risk of perinatal mortality, skilled management of patients with ESCRF at all stages of pregnancy contributes to the successful delivery in 40% - 75%.[4–15]

Clinical observation

The patient P, born in 1977, was supervised for chronic glomerulonephritis with the outcome to ESRD. Since 1994, she has been receiving RRT by PHD3 times a week using the dialyzer *lops 18* for 4 hours 30 minutes at a flow rate of 230 ml/min at the arteriovenous fistula of the right forearm. Composition of the dialysis solution: acetate (SW 449 A, 1+44) - Na+ 139 mmol/L, K+ 3.0 mmol/L, Ca++ 1.5 mmol/L, Glucose 1.0 g/L, Mg++ 0.5 mmol/L, chlorine 107 mg/L, HCO3- 36 mmol/L, CH3COO- 3.0 mmol/L; bicarbonate (Bic 8.4%) - NaHCO3 84.0 g/L. The past medical history features allotransplantation of a cadaveric kidney (1995), complicated by a cytomegalovirus infection and a crisis of rejection, repeated allotransplantation of a cadaveric kidney (ACK) in 1996. Among the illnesses she mentioned autoimmune thyroiditis, viral hepatitis B and C was recorded as a result of blood transfusion in 1994. Virus carrying is preserved. All previous pregnancies 2004, 2005, 2006 ended in induced abortionas the request of a woman.

In February 2013 the desired unplanned pregnancy was diagnosed at a gestational age of 6/7 weeks and was confirmed by laboratory monitoring of the level of human chorionic gonadotropin (HCG). At the time of pregnancy diagnosis anemia, mineral and bone disorders (MBD), liver performance indicators, dyselectrolytemia has not been detected: hemoglobin 121-116 g/L, total serum calcium 2.3 mmol/L, inorganic phosphorus 1.6 mmol/L, free parathormone 97.4 pg/ml, AST 10E/L, ALT 20E/L, total bilirubin 10.5 mmol/L, potassium 4.7 mmol/L, sodium 136 mmol, albumin 36.8 g/L. Urea and creatinine levels in serum reached 567 mcmol/L and 1.11 mmol/L respectively. The dialysis dose was adequate; regime of dialysis did not change (Kt/V Dialysis Dose (Daugirdas) = 1.39; Urea Reduction Ratio (URR) = 0.66).[16–18] Anticoagulation was 6000 U bolus type using low molecular weight heparin. The patient received routine therapy with calcium supplementation at a dose of 3 grams per day, L-thyroxin 25 mkg/day. Since the establishment of the fact of pregnancy, therapywas strengthened by appointment by vitamin E 400 mg/day, Folio-1 tablet/day, Utrogectan 300 mg/day per vaginum, Ketosteril 3 pills x 3 times/day.

At the gestational age of 9/10 weeks the frequency and duration of dialysis session was increased up to 6 times a week for 4 hours. Hemodiafiltration was not carried out due to patient's poor tolerability. Initial "dry" weight was 67 kg. According to the rate of weight gain of a healthy woman during pregnancy, the patient was corrected for the "dry" weight in200-400 ml weekly. At the gestational age of 12 weeks the first ultrasound screening was performed. According to fetometry: the parietal-coccygeal length (PCL) = 59mm, nuchal translucency (NT) = 1.4 mm. Clinical and laboratory monitoring of beta-HCG: 24920 IU/L (normal is from 20,000 to 90,000 IU/L or 13.4-128.5 ng/ml) - in the normal range. Pregnancy-associated plasma protein-A = 3.57 mU/ml (0.03-100 mU/ml). Herpesvirus type IV to the DNA copy 1.6x104 HHV6/ml, herpes zoster anti-VZV IgG to 1,696 mIU/mL, anti-phospholipin antibodies (IgG - 12.6 U/ml (0-4.5), IgM - 8.2 U/ml (0-4.5)) raising was recorded, as well as a positive result for the presence of antibodies to rubella and toxoplasmosis. Indicators of hepatitis B and C virus were within the normal range.

At the gestational age of 12 weeksa decrease in the hemoglobin level to 104 g/L has already been revealed. The therapy was enhanced with the addition of Epoetin-alfa (EPO) in a dose of 6000 U/week in combination with oral iron preparations (Ferrous sulphate+Ascorbic acid 200mg/day). From 14 to 16 weeks of pregnancy, despite attempts to correct anemia due to an increase in the dose of EPO and a change in the oral intake of iron for intravenous administration, the hemoglobin value was steadily declining. At the gestational age of 16 weeks the EPO dose was already 16.000 U/week, the hemoglobin level was 83 g/L. On the 17th week of pregnancy, taking into account the increase in ALT to 71-88 E/L, 5 heptral infusions of 400 mg daily were performed. Recommended strict adherence to dietary recommendations (diet number 5). Intravenous administration of iron preparations is replaced by oral. Progressing hypoalbuminemia (27.9 g/L) determined the tactics of correction of protein-calorie deficiency (PCD). Ketosteril was cancelled and a super protein was prescribed for 1 spoon 3 times/day. The ultrasound pelvic investigation at the gestation of 18 weeks showed the increase in amniotic fluid. The "dry" weight additions were stopped.

At the 21st week of gestation, the patient started having a yellowish-pink discharge in combination with a painful condition in the lower abdomen. According to the results of pelvic ultrasound monitoring an opening of the internal os, fetal bladders prolapsing to the cervix at 2.5 cm were diagnosed. In the uterus cavity, 1 fetus was detected in cephalic presentation, with a heart rate of 151 beats/min. Due to the high risk of preterm delivery inside the emergency medical aid (EMA) vehicle, the patient was delivered to a hospital where she was diagnosed with premature discharge of amniotic fluid, spontaneous abortion at 21 weeks and 3/7 gestation. According to the analysis of morpho-functional state of the placenta, acute placental insufficiency, immature placenta, focal purulent chorio-deciduitis were diagnosed. The genetic analysis of the fetus was not carried out. Anemia persisted -hemoglobin 85 g/L, PCD - albumin 26-23 g/L. After 7 days of hospitalization the patient was transferred to the Department of Gynecology of the All-Russian Center of Emergency and Radiation Medicine named after A.M. Nikiforov clinic No. 2 of the EMERCOM of Russia. Dialysis is returned to the original regime: 3 times a week for 4 hours 30 minutes, the antibiotic therapy was continued (Sultamicillin 1.5 g/day I.V. dripper No. 5), EPO therapy in a dose of 12.000 U/week in combination with iron supplementation (Ferric III hydroxide sacharose complex 100mg x 2 times/week). PCD was corrected by receiving 9 doses of albumin (20% 100ml № 9 x 3 times/week).

Over the next year the target hemoglobin level was reached, and therefore, the EPO therapy was cancelled. A psychologist repeatedly consulted the patient. On an outpatient basis, the patient was supervised by a gynaecologist with diagnose "Menstrual disorder, dysmenorrhea type". Ovarian dysfunction" (E28 at ICD-10). In 2015, at the patient's request, a comprehensive survey for preconception preparation was initiated. The dialysis dose was adequate; dialysis regime was not changed (Kt/V Dialysis Dose (Daugirdas) - 1.25; Urea Reduction Ratio (URR) - 0.68).[16–18] Anticoagulation was 6000 U bolus type using low molecular weight heparin. "Dry" weight = 66.0 kg. Clinical laboratory data: MBD - total serum calcium 2.2 mmol/L, inorganic phosphorus 2.4 mmol/L, free PTH 500 pg/ml, small dyselectrolytemia - potassium 5.3 mmol/L, sodium 133.4 mmol/L. Liver function indicators remained within normal limits - AST 25 U/L, ALT 29 U/L, total bilirubin 11.6 mmol/L; PCD not found - total protein 67 g/L, serum albumin 39g/L.

Thyroid hormones - in the normal range. Assessment of hormonal activity of the ovaries did not reveal pathology: lactation hormone - 305 mIU/L, estradiol - 285 pmol/L, luteinizing hormone - 19.6 IU/L (1.1-11.6), follicle stimulating hormone (FSH) - 8.2 IU/L (2.8-11.3), oncocytology smears - without atypia, minimum number of leucocytes (up to 5 in the field of view) in a smear for flora, mixed flora, STDs not found. According to ultrasound imaging of the lower pelvis: at the time of the study, the endometrium corresponded to the second phase of the MC, with the thickness of 7.0 - 8.0mm. Signs of diffuse changes in the myometrium, endocervical cysts. Comprehensive treatment at that time included calcium supplements at a dose of 3 grams per day, cinacalcet 30 mg/day, sevelamer 800 mg 4-6 pills/day, L-thyroxine 25mkg/day, Ketosteril 9 pills/day. Planned pregravid therapy included dydrogesterone on 16-25 days of the menstrual cycle monthly 10 mg x 2 times/day, "Femibion 1","Time Factor" vitamins during 3 months.

In order to prevent miscarriage and premature delivery the treatment was supplemented with dehydroepiandrosterone of 1 capsule every other day during 3 months. At the beginning of October 2015 the patient reported a delay in the planned menses for 7 days. According to the results of laboratory testing of the HCG level early pregnancy was diagnosed (HCG = 2012 mIU/mL). Correction of the dialysis and planned treatment was performed immediately: frequency and duration of dialysis sessions increased to 26 hours per week (4 hours and 30 minutes x 6 times a week). In order to prevent the development of hydramnios, the increase of the "dry" weight was not been performed. Sevelamer and cinacalcet therapy was canceled, started the taking of calcium citrate (Calcium citrate 1000mg + Magnesium citrate 500mg/Solgar/USA) at 1 pill/day. The level of hemoglobin was within 120 g/L. Anticipating-worsening anemia and development of fetal hypoxia, EPO therapy was started from 3000 U/every 10 days in combination with oral iron (Ferric III hydroxide sacharose complex 100mg x 2 times/week). Docosahexaenoic acid taking was initiated (Omegamama 2 pills x 3 times/day).

During the subsequent week the HCG level was monitored three times to confirm the progression of pregnancy (05.10.15-8173 mIU/mL, 08.10.2015-27442 mIU/ml, 12.10. 2015-62441 mIU/ml). Ultrasound pelvic investigation in the area of the uterus cavity diagnosed 1 ovum 13x10mm containing 1 fetus of 4 mm diameter, retrochorial hematoma. Gynecological examination with ultrasound pelvic was conducted 1 time every 10 days. The therapy was reviewed: dydrogesterone 10 mg x 3 times a day, progesterone 200 mg x 2 times per day, Femibion 1 pill/day. With increasing frequency and duration of dialysis sessions the patient's condition worsened after 2 hours from the beginning of dialysis. Negative dynamics in the

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form of increasing in heart rate up to 90-110/min and breathing acts till 19-20/min, anxiety was observed. Potassium level - 3.7 mmol/L. Given the lack of effect of diet therapy (raisins, dry apricots, grapes, bananas, tomato juice, etc.) solutions of potassium and magnesium asparaginate (Panangin) were added to the treatment 10ml to 100ml Sol. NaCl 0.9% I.V. dripper. As a result, the patient's condition improved significantly.

On the 5th/6th week of pregnancy, hemoglobin decreased to 114 g/L and ferritin rose to 1134 mcg/L. The dose of EPO was increased to 3.000 U/week and the oral iron is reduced to 100 mg/day. It should be noted that the leucocytosis detected at this time - 10.3 x 10^9/L - was maintained throughout the entire pregnancy. The ultrasonic monitoring at this stage did not reveal any signs of retrochorial hematoma. At the gestational age of 12 weeks one fetus was diagnosed. No rough congenital malformations and sonographic markers of chromosomal aberrations were found. The heartbeat was rhythmic, heart rate was 166 beats/min. According to fetometry: Parietal-coccygeal length = 52 mm (Snijders RJM), head circumference = 60mm (Hadlock), hip thickness = 5mm (Demidov), abdominal circumference = 55mm (Hadlock), RTA = 1.9mm, visualization of the nasal bones - to be determined. Fetus dimensions correspond to 11-12 weeks of pregnancy. The ductus venosus PI = 1.1, the tricuspid valve was in the normal range. Amniotic fluid was in the normal range. Chorionic villi was located on the rear surface of the uterine wall. The length of the cervical canal (CC) was 37 mm. The internal os was not expanded. Myometrium had homogeneous structure, the nodes were not visible.

At the 14th week of gestation in connection with a progressive anemia - hemoglobin 105 g/L - the dose of EPO is increased to 6 000 U/week. Also was diagnosed with cholestasis of pregnancy - AST 40 U/L, ALT 91 U/L. Hepatoprotective therapy included Heptral infusion at 400 mg I.V. dripper No. 5, with subsequent transition to Essentiale 600mg at 2 capsules x 2 times/day, therapy of keto-aminoacids canceled and started with super protein at a dose of 3 spoons/day. Femibion-1 replaced in to Femibion-2 in dose of 1 tabl/day. Oral pharynx staphylococcal infection (staphylococcus aureus) has been identified. For the purpose of sanitation of the oral and nasal cavities, an oil solution of Chlorophyllin, Stomatofit and Derinat was used. Oral pharynx and nasal test inoculation did not include pathological microflora growth further. At the 16th week of gestation anemia increased – hemoglobin 97 g/L and cholestasis - AST 49 U/L, ALT 151 U/L. Another correction of drug therapy included: increased dose of EPO 12000 U/week and Progesterone up to 200mg x 3 times/day and vitamins (Omegamama) was canceled.

At 17th week gestation during a follow-up pelvic ultrasound monitoring the uterine tonus was normal, fetal movement remained active. Attention was paid to the dynamic shortening of the cervix by 6 mm. Negative dynamics manifested itself within two weeks: 36.0 → 30.9 mm in combination with the opening of the upper third of the cervical canal to 6.0 mm. From 18th till 22th week's gestation the patient was being treated in the department of gynecology at the All-Russian Center of Emergency and Radiation Medicine. The motion behaviour was limited to II – bed rest.[7] At 23 week of gestation given the high risk of preterm delivery the patient was again admitted to the obstetric clinic with a diagnosis of "Ongoing pregnancy week 23/24. Insuficiencia istmicocervical. Hydramnios". Gradual shortening of the cervix in combination with the expansion of the internal os.

In order to prevent the syndrome of respiratory distress, the fetus performed 4 intramuscular injections of dexamethasone 12 mg at intervals of 12 hours. The second course was held 2 weeks later. At 27/28 weeks gestation - 03.03.2016 - in connection with the beginning of premature birth, cesarean section in the lower uterine segment was performed. We extracted a live aborted fetus male weighing 970 grams, length 35 cm, and autonomous respiration. Apgar score: 5/6 points. No postpartum complications were noted. The patient was discharged on the seventh day after birth in a satisfactory condition with the recommendations following the diagnosis: Pregnancy 27-28 weeks. Insuficiencia istmicocervical. Hydramnios. Premature delivery. Chronic glomerulonephritis. Terminal chronic kidney disease. The child was transferred to Children's City Hospital No. 1 for further observation and treatment. At the age of four months the boy was discharged in satisfactory condition with a weight of 3 kg 600 grams under the supervision of a paediatrician, a neurologist, a pulmonologist at the place of residence.

Discussion

The case features qualified care and treatment in a specialized hemodialysis department of the EMERCOM of Russia in St. Petersburg for a patient aged 39 years with chronic kidney disease (CKD) and pregnancy, starting with a preconception preparation. Chronic glomerulonephritis with the outcome to CKD was diagnosed since the patient was 17 y/o. The first pregnancy in the patient was diagnosed at the age of 27 years against the backdrop of a 10-year period of dialysis therapy, which contributed to the normalization of the most important functions of the body, including reproductive. This is evidenced by the fact of overcoming infertility (medical abortions 2004, 2005, 2006, late spontaneous abortion at the 21 week period). At the time of the beginning of the pregravid preparation, the duration of the prolonged dialysis therapy was 22 years. Since 1994 hemodialysis treatment of the patient hasn't changed. At the present time we have obtained the results of many comparative studies of the quality of PHD and HDF therapy.[17,19] Despite the results obtained worldwide, in our dialysis department patients receive hemodiafiltration therapy strictly according to indications.[19]

In 2013 with the onset of pregnancy the patient was transferred to hemodiafiltration therapy. We changed the dialysis membrane from low flux to high flux and increased bloodflow from 230 to 300 ml/min led to a sharp deterioration in the patient's condition. This was manifested by destabilization of hemodynamics in the form of jumps in bloodpressure during the dialysis procedure and an extension of the recovery period after the end of the procedure. Given the deterioration in the quality of life of the patient using hemodiafiltration, inorder to preserve and prolong the pregnancy, our attempt stotre at hemodiafiltration were stopped and did not recur. It is known that the prognosis of pregnancy outcome for the mother and fetus with CKD is doubtful or unfavourable.[1,2,17,20,6,21,22] Such women should be under the supervision throughout the pregnancy. According to the Ministry of Health and Social Security of the Russian Federation order No. 731 from 2007, CKD of any ethiology (N 18. 9) is a medical indication for an induced termination of pregnancy. The level of blood serum creatinine prior to conception for any diagnosis in patients with CKD should not exceed 200 mmol/L (1.8 mg/dL). The progressive increase in serum creatinine in any period of pregnancy requires immediate termination.

The patient totally refused to interrupt the pregnancy, which occurred after the preconception preparation. In the process of dynamic monitoring, adequate correction of both dialysis and planned drug therapy was conducted.[23,24,25,26,22] Kt/V level of the pregnant patient with daily dialysis session was not less than 1.2 during all period for the whole observation period. We suppose that the patient has poor

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URR because of the large fluid losses during dialysis session (3.5-4.0 liter spersession).[1,2,17,20,18,19] Changes of the blood volume during ultrafiltration by suprasonic technique of the blood line were not used. The patient's mode of ultrafiltration was constant ultrafiltration. Before the pregnancy the patient received iron preparations as needed. Hemoglobin level was within the target level (120 g/L). Epoetin alfa was not used. This clinical case confirms the high frequency of pregnancy complications, starting already at 12 weeks: cholestasis of pregnancy, anaemia. In 2013, during pregnancy, the patient received irontherapy, but inview of the appearance and increase of cholestasis in combination with chronic hepatitisinfection, on there commendation of a gynecologist, many drugs, including ironpreparations, were canceled. Also, epoetin alfa therapy was not started ontime, which led to anemia, which arose and grows indynamics. In 2015, during these conddesired pregnancy, we took into account the available initial experience.[27–31]

In 2016 starting at 16-17 weeks gestation cervical insufficiency is formed. Closure of the cervix reduces the incidence of preterm delivery, up to 33 weeks, according to the references. In this case, a contraindication to surgical treatment of the cervical insufficiency is the disease that is a contraindication to the preservation of pregnancy, in particular, CKD. Continued conservative therapy preserves pregnancy at 23-24 weeks in the third level obstetric clinic allowed to prolong for 5 more weeks, prevent the respiratory distress syndrome of fetus using glucocorticoids. The optimum method of delivery was caesarean section. As a result the mother and the child were discharged in satisfactory condition after 7 days and 4 months respectively.

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In obstetrical practice, cases of refusal to interrupt pregnancy with women with severe somatic pathology, which is a contraindication to pregnancy, are not uncommon because of the high risk of maternal and perinatal morbidity and mortality. The description of this clinical case makes us think about reviewing the views and tactics of administering patients of childbearing age with ESRD to PGD and to focus on creating teams of like-minded doctors aware of their responsibility for fulfilling the most cherished dream of every woman - the birth of a child. The analysis of this case allowed us to formulate the main points in the work with this category of patients. First, the desire of a woman to become a mother persists despite the prohibitions and warnings of dialysis physicians. In the case of a woman's conscious desire, pregnancy planning and mandatory pregravid preparation for conception are necessary. It includes the following:

i. Examination and observation by a gynaecologist in conjunction with possible correction of therapy

ii. Comprehensive laboratory and instrumental examination (ECG, ECHO-KG, chest X-ray of both partners, ultrasound of the abdominal cavity and pelvis, urine culture in the presence of residual renal function, sowing from the throat and nasal cavity).

iii. Consultation of the dentist.

iv. Therapeutic and/or surgical treatment of all available chronic foci of infection.

v. Secondly, early monitoring of the fact of pregnancy, namely the control of serum HCG with a delay in planned menses for 2-3 days or more and the performance of ultrasound. Control of ultrasound of the pelvis should be performed at least once every 10 days throughout the pregnancy, while paying special attention to the size of the cervix and cervical canal.

Thirdly, in the case of early pregnancy diagnosis, a transition to daily hemodialysis of a total duration of at least 24 hours per week is necessary. It is preferable to conduct hemodialysis therapy in combination with hemodiafiltration with its satisfactory tolerability. Do not forget that the minimum content of potassium in the dialysis solution should be at least 4.0 mmol/l. According to the indications during the dialysis session, it is possible to perform infusion therapy with the use of potassium preparations. In order to correct diselectrolithy, it is necessary to prescribe combined therapy with calcium and magnesium preparations. Particular attention should be given to early initiation of therapy with erythropoietin for the prevention and treatment of anemia. In our case, EPO therapy is started at a haemoglobin level of 120 g/l.

Conclusion

I would like to note the fact that from 16 to 18 weeks, in order to maintain and prolong pregnancy, strict restriction of physical activity of a woman is necessary, by mandatory stay in a specialized obstetric-gynaecological hospital.

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