Clinical Case Report

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Successful pregnancy and delivery in uremic patients with maintenance hemodialysis

A case report

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Abstract

Rationale: It is reported that successful pregnancies in dialyzed uremic women are rare. Over the past years, despite advances in clinical management and technology in dialysis for pregnancy in patients receiving maintenance hemodialysis, uremia remains a high risk factor for adverse outcomes in mother and fetus.

Patient concerns: In this article, we present a case of pregnancy in a 34-year-old uremic woman on dialysis. After the pregnancy was diagnosed and confirmed, intensive dialysis and multidisciplinary care according to the recommendations in the available literatures were provided.

Diagnoses: Single pregnancy of 31^{+4} GWs (gestational weeks), fetal growth restriction, polyhydramnios, and uremia.

Outcomes: At 31 weeks' gestation and 4 days, she was admitted to our hospital due to premature rupture of membranes and abdominal pain. Then a female baby weighed 1700 g was delivered successfully. After one year of follow-up, the mother feels well and the baby is healthy.

Lessons: Intensive dialysis, detailed management and multidisciplinary approaches are necessary for optimal outcomes in uremic pregnant mother and fetus.

Abbreviations: ACEI = angiotensin-converting enzyme inhibitors, ARB = angiotensin receptor blockers, BUN = blood urea nitrogen, CKD = chronic kidney disease, CRRT = continuous renal replacement therapy, cTnI = Troponin I, GWs = gestational weeks, Hb = hemoglobin, HCG = human chorionic gonadotrophin, HCT = hematocrit, MHD = maintenance hemodialysis, Scr = serum creatinine.

Keywords: chronic kidney disease, hemodialysis, pregnancy, uremia

1. Introduction

Compared to normal women, pregnancies in uremic patients undergoing maintenance hemodialysis (MHD) have a higher risk of adverse outcomes in mother and fetus, such as spontaneous abortion, hypertension, pre-eclampsia, polyhydramnios, preterm labor, and premature birth.[1] Since the first case of pregnancy and successful delivery of MHD patients in the world in 1970s, with the continuous development and improvement of dialysis technologies and experiences, more and more successful cases have been reported, but reports in China are rare.[2] Last year, the first successful pregnancy and delivery in a uremic patient with MHD was admitted to our blood purification center, which has a history of over 40 years. During one year of follow-up, the mother feels well, and the baby is also in good health. The written informed consent was obtained from the patient and ethical approval was given by the medical ethics committee of Affiliated Hospital of Nantong University.

2. Case presentation

A 34-year-old G5P1 woman whose last menstrual period was on 16 September, 2016, had received uremia maintenance hemodialysis for 4 years; she was diagnosed with pregnancy by pelvic ultrasound after approximately 16 weeks of amenorrhea. She had an underlying disease of chronic glomerulonephritis (CGN). The timeline of the patient care was shown in Figure 1.

During the past years before pregnancy, the dialysis scheme of the uremic woman was 4-hour dialysis sessions 3 times weekly, and then the intensive dialysis and multidisciplinary cooperation according to the recommendations in the available literatures were performed on the pregnant woman. Firstly, the total weekly hemodialysis increased from 12 to 20 hours, the dialyzer with high efficiency biocompatible membrane was used, the average blood flow was from 180 to 240 mL/min and the dialysate flow was 500 mL/min. Low-molecular weight-heparin (bolus dose of 1000 IU followed by 250 IU every hour) was used to minimize the hemorrhagic risk and avoid coagulation of the dalyzer. Secondly, control of dry weight by slow continuous ultrafiltration in order

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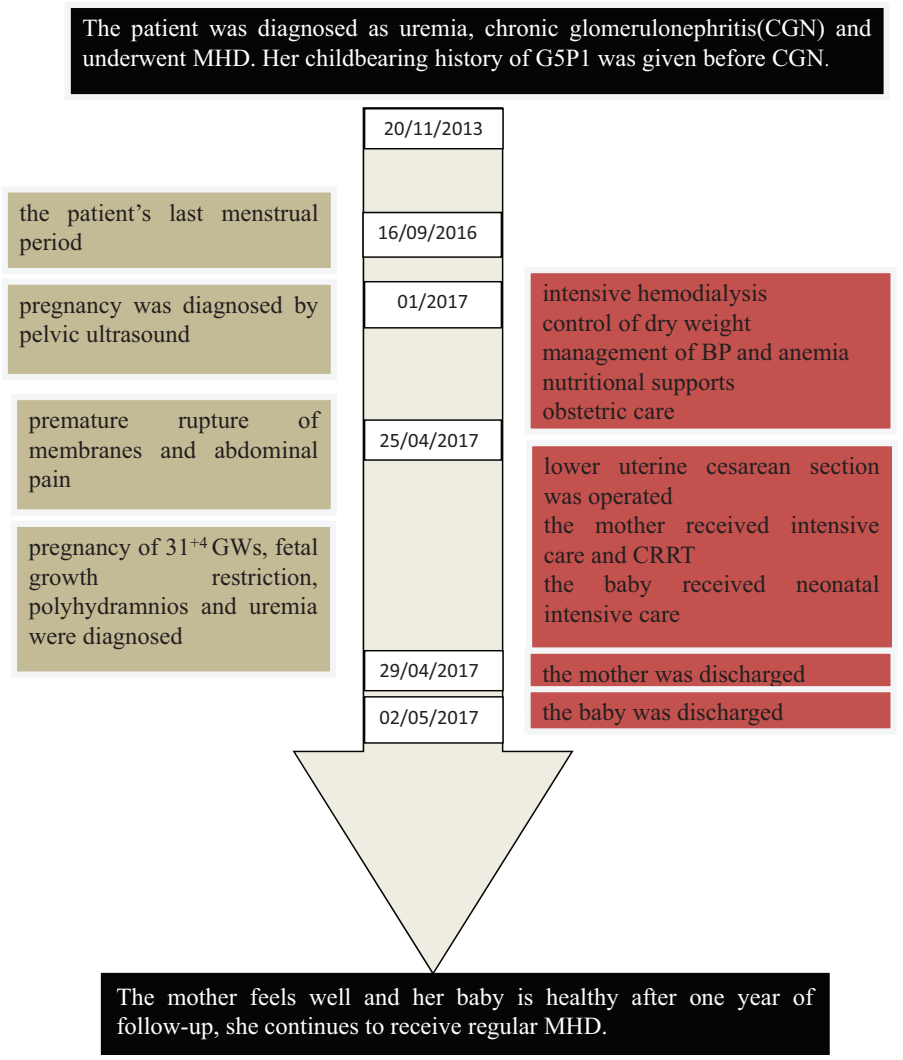

Figure 1. The timeline of the patient care.

to achieve the goal of 0.5 kg on weight gain per week. Thirdly, in order to target the postdialysis blood pressure below 140/90 mm Hg and to avoid intradialytic hypotension (<120/70 mm Hg), the dialyzed pregnant woman was treated by combination of ultrafiltration assessments and antihypertensive drugs, including long-acting calcium antagonist and alpha-methyldopa. Fourthly, management of anemia. The patient received subcutaneous recombinant human erythropoietin at a dose of 10,000 international units twice per week and intravenous iron administration of iron sucrose at a dose of 100 mg biweekly, as well as 10 mg of folic acid supplementation. In addition, nutritional supports were also performed on the pregnant women as follows: protein intake of 1 g/kg/d and 20 g/d more, calorie intake of 35 to 40 kcal/d. The dose of intake for calcitriol and calcium carbonate D3 was 0.25 μg/d and 0.6 g/d, respectively. With regard to the obstetric care, after the pregnancy was confirmed by pelvic ultrasound, the fetal biometries were assessed scheduled according to obstetric doctor's advice. The single umbilical artery, polyhydramnios and fetal growth restriction and no other abnormalities were found. After the management of the pregnant women on hemodialysis, her blood tests showed the hemoglobin (Hb) levels ranged from 9 to 11 g/dL, hematocrit (HCT) ranged from 25% to 30%, blood urea nitrogen (BUN) level was between 14.5 and 25 mmol/L and serum creatinine (Scr) was in the range of 804 to 1180 μmol/L, the calcium and phosphorus levels were kept in the normal range.

In April 25, 2017, at 31 weeks' gestation and 4 days more, she was admitted to the obstetrics and gynecology department due to premature rupture of membranes and abdominal pain for 9 hours. Physical examination: *T*: 36.2°C, *P*: 106 beats/min, *R*: 18 beats/min, BP: 156/97 mm Hg. Abdominal ultrasound showed single live pregnancy, fetal heart rate was 144 beats/min, fetal growth restriction, and polyhydramnios (amniotic fluid index was 24). Her blood were examined: WBC: 10.1×10^9/L, N: 89.1%, L: 6.8%, RBC: 2.15×10^{12}/L, Hb 73 g/L, HCT: 0.22 L/L, PLT: 237×10^9/L. ALT: 10 U/L, AST: 16 U/L, total protein: 57.2 g/L, albumin: 34.9 g/L. BUN: 19.2 mmol/L, Scr: 862 μmol/L, UA: 443 μmol/L. K^+: 4.1 mmol/L, Na^+: 140 mmol/L, Cl^-: 100 mmol/L, Ca^{2+}: 2.16 mmol/L, P^{3+}: 2.18 mmol/L. Troponin I (cTnI) 0.729 μg/L. The left ventricular ejection fraction (LVEF) measured by color Doppler echocardiography was 0.59. Enlargements of left atrium and left ventricle, as well as slight of mitral regurgitation were detected. She was diagnosed with single pregnancy of 31^{+4} GWs (gestational weeks), fetal growth restriction, polyhydramnios and uremia.

Then under general anesthesia, lower uterine cesarean section was performed and a female baby weighed 1700 g was delivered successfully. The baby, whose apgar scores were 8 at first minute and 10 at 5th minutes was sent to the neonatal intensive care unit because of her respiratory distress. And then she was discharged healthy after one week of intensive care. After the operation, the mother was sent to intensive care unit, hemodynamics monitor, ventilator-assisted breathing, continuous renal replacement therapy (CRRT) and other support therapy were performed. Four days later the mother's status was stable and she was discharged. Subsequently, she continued to receive regular dialysis. In the one year of postpartum follow-up, complications were not found in both the mother and the baby.

3. Discussion

In general, the rate of pregnancy in dialyzed women with uremia in their childbearing age is lower than normal women. However, once pregnancy during dialysis is confirmed, it is a great challenge for the mother, fetus, nephrologist and obstetrician. It is estimated that early chronic kidney disease (CKD) is present in about 3% of pregnant women and that 1:750 pregnant women are involved in advanced CKD (stage 3–5).[3] In a survey among nephrologists in Germany, about 45% of the doctors routinely provided contraception counseling and pregnancy guidance on the women undergoing MHD, 22% of them would suggest terminating pregnancy after the conception, whereas only 40% of all the respondents felt confident in dealing with pregnant women on dialysis.[4] Similarly, the survey in America indicated that 46% of nephrologists and their staffs offered contraception counseling, 37% stated they would recommend termination of pregnancy in dialyzed women, and 30% felt some uncomfortable to treat dialyzed pregnant women.[5] On the basis of these results, more attention should be paid in the diagnosis and treatment of pregnancy in women on dialysis.

Due to ovarian dysfunction, menstrual cycle disorders, and even amenorrhea, pregnancy in MHD women is not easy, it is also not easy to detect early after pregnancy. In women on dialysis, the diagnosis of pregnancy is often delayed; it takes until about 16.5 weeks of pregnancy to make a correct diagnosis.[6] During uremia, reduced urinary human chorionic gonadotrophin (HCG) excretion usually causes abnormal increase of blood HCG, so it is unreliable to confirm pregnancy through the HCG level in blood. Ultrasound examinations are regarded as the most reliable method for clinical diagnosis of pregnancy and calculate the gestational age in MHD patients.[7,8] Consistent with these data, the patient was also diagnosed with pregnancy in mid-gestation but had a successful delivery. Therefore, it is necessary to provide contraception and prenatal education for the sake of both mother and fetus as soon as possible.

In spite of advance in management of pregnancy during MHD, adverse maternal and fetal outcomes remain high; approximately 80% of the pregnant women will suffer from hypertension and half of the hypertensive patients may lead to eclampsia.[5,9] First-line antihypertensive drugs are commonly used for pregnancy hypertension include methyldopa, labetalol, and nifedipine.[6,10] The target of antihypertensive management is below 140/90 mm Hg while dialysis hypotension (<120/70 mm Hg) should be avoided.[10] Both angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) may cause intrauterine growth restriction, oligohydramnios, pulmonary hypoplasia, and fetal death, and hence are contraindicated during pregnancy.[11] Anemia is common in pregnant women with uremia. Furthermore, maternal anemia during pregnancy is an independent risk factor for low-birth weight and preterm delivery.[12] In order to maintain target Hb levels of 10-11 g/dl and HCT levels of 30% to 35%, the dosage of intravenous iron and erythropoietin requirements usually need to be increased.[9] In this case, the maternal Hb was not up to the goals and may be associated with the predialysis test and increased blood volume. Polyhydramnios is another common complication in pregnant women receiving HD, it is found in 30% to 70% of dialyzed women with uremia.[9] As far as the risks to the fetus are concerned, besides abortion or stillbirth, more than 80% of infants are premature, with an average gestational age of 32 weeks.[13] Consistent with these results, the mother was associated with polyhydramnios and gave birth to a premature baby in our case.

Over the past 20 years, a growing body of evidence has been showed that intensive HD improves maternal and fetal outcomes, especially for the rise of successful birth rate.[10,14] In a cohort comparison, Hladunewich et al[14] found that the live birth rates for pregnant women receiving less than 20 hours of HD per week was only 48%, whereas this rate would increased to 85% when they were dialyzed more than 36 hours in a week. A meta-analysis indicated that intensive hemodialysis (3.5–4 h/session, 5-6 times/week) could significantly reduce the preterm birth rate in pregnant women on HD (pregnancy < 37 w, $P = .044$) and the percentage of newborns with low-birth weight ($P = .017$).[13] In United States, the nephrologists generally prescribe 4 to 4.5 hours of HD 6 days/week or an average of 23 ± 7 h/week for pregnant women on dialysis.[5] Therefore, intensive hemodialysis is regarded as the standard regime of care for dialyzed women on pregnancy.[6,9,10,13,15,16] In addition, intensive dialysis lower maternal urea levels as much as possible, reduce fetal-osmotic diuresis and polyhydramnios, and avoid rapid fluid shifts, and fetal distress.[7] It is recommended that predialysis urea nitrogen levels in maternal blood should below 50 mg/dL (17.9 mmol/L) or urea levels below 100 mg/dL (16.6mmol/L).[6,7]

Despite intensive hemodialysis, it is very important to maintain the stability of maternal environment for the growth of fetus. Weight gain between sessions and dry weight during pregnancy should be carefully monitored in order to avoid excessive hyperfiltration caused by uteroplacental hypoperfusion and fetal distress.[7] Moreover, dry weight should be adjusted according to the growth and development of the fetus during pregnancy. It is appropriate for dry weight to increase by 1 to 1.5 kg in the first trimester of pregnancy and then increase from 0.45 to 1 kg/week.[6,9] In order to avoid hypokalemia and alkaliemia, the concentrations of 3 to 3.5 mmol/L potassium, 25 mEq/L bicarbonate, and 2.5 mEq/L calcium in dialysate are preferred.[9] The nutritional status of pregnant women on dialysis is a critical factor for fetal development, for this reason, intake of 1.2 to 1.4 g/kg/day and additional 20 g/d protein, and total 25to 35 kcal/d calories are recommended for pregnant patients.[6] In addition, supplementation of sufficient folic acid, calcium, and vitamin D analogs are considered safe in pregnancy. Vitamin D and calcium levels should be monitored and kept in the lower normal range.[6]

The theme of World Kidney Day in early this year was focused on women and kidney disease.[17] Pregnancy on uremic women undergoing dialysis is a special state that needs to be highly valued. Management of pregnant women on dialysis is a challenge for the nephrologists, obstetrician, and nutritionist. Up to now, there are few data to guide best practice in the area. Live birth rates in pregnant women on hemodialysis are improving and up more than 80% by using intensified hemodialysis regimens during pregnancy.[16]

Management of dialyzed women with uremia in their childbearing age should include pregnancy. Preconceptional counseling, greater attention and earlier diagnosis of pregnancy, and then intensive dialysis, better control of blood pressure, correction of anemia, management of diets, obstetric monitor and neonatal care are all contributed to the pregnancy outcomes. Multidisciplinary co-operations among nephrologists, obstetricians, nutritionists, and other caregivers are also important in order to ensure optimal results. In future, further researches that focus on dedicated interventions and education programs to improve pregnancy outcomes are needed.

Author contributions

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References

[1] Kendrick J, Sharma S, Holmen J, et al. Kidney disease and maternal and fetal outcomes in pregnancy. Am J Kidney Dis 2015;66: 55–9.
[2] Yu P, Diao W, Tang Q, et al. A successful pregnancy and parturition in a patient with anuria undergoing maintenance hemodialysis for 6 years: a case report of a 3-year-follow-up. BMC Pregnancy Childbirth 2015; 15:218.
[3] Williams D, Davison J. Chronic kidney disease in pregnancy. BMJ 2008;336:211–5.
[4] Duffner J, Schulte-Kemna L, Reister B, et al. Survey among nephrologists in Germany: current practice and management of pregnant women on dialysis. Clin Nephrol 2017;88:264–9.
[5] Sachdeva M, Barta V, Thakkar J, et al. Pregnancy outcomes in women on hemodialysis: a national survey. Clin Kidney J 2017;10:276–81.
[6] Manisco G, Poti M, Maggiulli G, et al. Pregnancy in end-stage renal disease patients on dialysis: how to achieve a successful delivery. Clin Kidney J 2015;8:293–9.
[7] Fitzpatrick A, Mohammadi F, Jesudason S. Managing pregnancy in chronic kidney disease: improving outcomes for mother and baby. Int J Womens Health 2016;8:273–85.
[8] Cabiddu G, Castellino S, Gernone G, et al. Best practices on pregnancy on dialysis: the Italian Study Group on Kidney and Pregnancy. J Nephrol 2015;28:279–88.
[9] Furaz-Czerpak KR, Fernandez-Juarez G, Moreno-de la Higuera MA, et al. Pregnancy in women on chronic dialysis: a review. Nefrologia 2012;32:287–94.
[10] Hladunewich M, Schatell D. Intensive dialysis and pregnancy. Hemodial Int 2016;20:339–48.
[11] Piccoli GB, Cabiddu G, Attini R, et al. Hypertension in CKD pregnancy: a question of cause and effect (cause or effect? This Is the question). Curr Hypertens Rep 2016;18:35.
[12] Levy A, Fraser D, Katz M, et al. Maternal anemia during pregnancy is an independent risk factor for low birthweight and preterm delivery. Eur J Obstet Gynecol Reprod Biol 2005;122:182–6.
[13] Piccoli GB, Minelli F, Versino E, et al. Pregnancy in dialysis patients in the new millennium: a systematic review and meta-regression analysis correlating dialysis schedules and pregnancy outcomes. Nephrol Dial Transplant 2016;31:1915–34.
[14] Hladunewich MA, Hou S, Odutayo A, et al. Intensive hemodialysis associates with improved pregnancy outcomes: a Canadian and United States cohort comparison. J Am Soc Nephrol 2014;25:1103–9.
[15] Alkhunaizi A, Melamed N, Hladunewich MA. Pregnancy in advanced chronic kidney disease and end-stage renal disease. Curr Opin Nephrol Hypertens 2015;24:252–9.
[16] Tangren J, Nadel M, Hladunewich MA. Pregnancy and end-stage renal disease. Blood Purif 2018;45:194–200.
[17] Piccoli GB, Alrukhaimi M, Liu ZH, et al. World Kidney Day Steering CWomen and kidney disease: reflections on world kidney day 2018. J Ren Care 2018;44:3–11.