Development of hypertensive complications in oocyte donation pregnancies: from bench to bedside

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CHAPTER 7

Significance of specialized preconception counseling in oocyte donation pregnancy with prior history of postpartum eclampsia

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ABSTRACT

A well-known complication in oocyte donation (OD) pregnancy is preeclampsia. Here, we present a 31-year-old woman, pregnant after OD. She conceived by the reception of the oocyte from her partner (ROPA) and sperm from a sperm donor. She developed preeclampsia with severe features, necessitating caesarean delivery at 29 weeks' gestation due to deterioration of her clinical condition. Admission at the intensive care unit postpartum was necessary, because of recurrent postpartum eclampsia and administration of high dose magnesium sulphate for convulsion prophylaxis. This case illustrates the importance of preconception counseling for patients who are considering to conceive by OD and double gamete donation. In this specific case an alternative way to conceive was available. However, ROPA was preferred as part of shared lesbian motherhood. The risk of complications in the subsequent pregnancy has led to an alternative decision to accomplish a second pregnancy.

BACKGROUND

In shared lesbian motherhood, a woman conceives by the reception of the oocyte from her partner (ROPA) and donated sperm. (1) This form of assisted reproduction is technically indistinguishable from oocyte donation (OD), using the assisted reproduction technique (ART) of in vitro fertilization (IVF) with a donated oocyte. OD pregnancies have a higher risk of developing hypertensive complications compared to non-donor pregnancies. (2-5) Consequently, women who wish to conceive as part of shared lesbian motherhood by ROPA need to be counseled in detail about the risks of the ART, as well as the risks of complications associated with OD. The following case describes a couple with a pregnancy through shared lesbian motherhood complicated by early-onset preeclampsia with severe features and postpartum eclampsia. They returned to our outpatient clinic one year after delivery with a wish for a second pregnancy.

CASE PRESENTATION

Our patient, 31 years old, conceived by using ROPA and sperm from a sperm donor. This was her first pregnancy, and was checked under midwifery care. At the gestational age of 27 weeks and 2 days she consulted our gynaecology department at the Leiden University Medical Center (LUMC, the Netherlands), because of headache and scotomas. She was admitted with a blood pressure of 130/90 mmHg, normal liver and kidney function, platelet count 166·109/L, uric acid 0.40 mmol/L, and no proteinuria. With ultrasound testing, a fetus in cephalic position was observed with growth according to the 30th percentile. The patient was discharged the next day with stable blood pressure and no development of proteinuria. Two weeks later she was re-admitted because of headache, dyspepsia, dyspnoea and scotomas. She had gained 4 kg of weight in the last weeks and her blood pressure had increased to 160/100 mmHg.

INVESTIGATIONS

The laboratory tests demonstrated: haemoglobin 8.9 mmol/L, haematocrit 0.417 L/L, uric acid 0.49 mmol/L, AST 78 U/L, ALT 65 U/L, platelets 149·109/L, a urine protein/creatinine ratio of 889.2 mg/mmol, and proteinuria of 5.92 g/24 hours.

TREATMENT

After admission, magnesium sulphate 1 g/hour after a bolus of 4 g, as prevention for eclamptic insults, and antihypertensive medication (Labetalol 20 mg/hour) were administered intravenously. Moreover, the patient received corticosteroids (Celestone:

β-methasone (3 mg) disodium phosphate and β-methasone (2.7 mg) acetate) to stimulate the development of the fetal lungs. The first administration of Celestone was 27 hours before delivery, and the second administration 3 hours before delivery. In the following days her condition worsened: she developed dyspnoea, the headache worsened, and her blood pressure increased again to 175/120 mmHg. Consequently, we performed a caesarean section at 29 weeks' gestation and a male infant of 1395 g was born with Apgar scores of 4, 6, and 8 at respectively 1, 5, and 10 minutes. Her blood pressure remained stable with antihypertensive medication (Labetalol 20 mg/hour). The next day however, she developed eclamptic convulsions despite of increasing dosage of magnesium sulphate (2 g/hour, and four times the administration of a 2 g bolus; magnesium level 3.05 mmol/L). The dosage of Labetalol was gradually increased to 100 mg/hour. However, the eclamptic convulsions did not decrease despite the high dosage of magnesium sulphate, so the patient was admitted to the intensive care unit for sedation and intubation during two days. The administration of magnesium sulphate was stopped four days after delivery. Nine days after her delivery, she was able to leave the hospital in good clinical condition. Six weeks later, at the postpartum check-up, the patient did not have any preeclamptic symptoms, and her blood pressure was 100/60 mmHg.

OUTCOME AND FOLLOW-UP

A year later, the patient and her partner returned to our outpatient clinic with a wish for a second pregnancy. This partner suffers from a stable chronic kidney disease stage 2 with a dysplastic kidney. In addition, she has a mild hypertension, which is controlled with a daily dose of 25 mg of Losartan potassium. Because of the recent complicated pregnancy of the patient, the existing comorbidity of her partner, and the new pregnancy wish with available cryopreserved embryos, specialized preconception counseling was scheduled.

Preconception counseling

During this counseling we discussed the risk of recurrence of preeclampsia and the alternative methods for conception. The following options were mentioned:

Achieving pregnancy of the partner using:
1. the residual cryopreserved embryos,
2. insemination,

Achieving pregnancy of the patient using:
3. the residual cryopreserved embryos,
4. insemination with sperm of a new donor,
5. insemination with sperm of the previous donor.

First, the risk of developing hypertensive complications in the following pregnancy was discussed. An IPD meta-analysis from 2015 shows a recurrence risk of 20.4% (95% CI 20.4-

20.9) for women with preeclampsia in their medical history. With a gestational age under 34 weeks, the recurrence risk for hypertensive pregnancy complications is 36%. (2) In general however, the course of hypertension is milder at recurrence.

Oocyte donation and pregnancy complications

The risks of a second OD pregnancy were discussed, while cryopreserved embryos were stored at the fertility clinic. A recent published systematic review and meta-analysis showed that the risk of developing preeclampsia in OD pregnancies compared to non-donor ART pregnancies is increased (OR 2.11; 95% CI 1.42-3.15). This also applies to the risk of developing pregnancy induced hypertension (OR 2.30; 95% CI 1.42-3.32). When OD pregnancies are compared to naturally conceived pregnancies, the risk for preeclampsia is even more increased (OR 2.94; 95% CI 2.29-3.76). (3) In this meta-analysis, stratification for multiple pregnancy was performed. Regarding maternal age, the individual studies corrected independently by multivariate analysis, stratification or matching. In addition to hypertensive complications, OD pregnancies have an increased risk of spontaneous miscarriage, preterm birth and low birthweight. (3, 4, 6) Moreover, OD pregnancies end more often in a caesarean section and there is an increased risk of haemorrhage postpartum. (5, 6) In OD pregnancies, the fetal genome can be totally allogeneic to that of the mother, since the fetus obtains genes from the father and donor. Possibly, due to this high level of immunogenic dissimilarity a different immunoregulation of the maternal immune system and pathological placentation occurs, consequently causing the hypertensive complications. (5, 7) The immunogenic dissimilarity is reflected by the number of Human Leukocyte Antigen (HLA) mismatches. The HLA haplotypes are co-dominantly expressed and a child inherits a haplotype of each parent. Hence, the chance that the patient is exposed to a totally allogeneic fetus in her second OD pregnancy, using the same oocyte donor and donor sperm, is 25% compared to 0% in an autologous pregnancy. Based on this theory, the recurrence risk of preeclampsia could be increased in an OD pregnancy.

Shared lesbian motherhood and pregnancy complications

Previous research found that using donor sperm is also associated with an increased risk of preeclampsia (OR 1.63; 95% CI 1.36-1.95). (8) Since shared lesbian motherhood requires double gamete donation by using ROPA and donor sperm, this could imply an even higher risk for preeclampsia than OD alone. In a retrospective cohort study, Blazquez *et al.* found a higher risk of preterm preeclampsia in double gamete donation compared to OD alone (OR 3.02; 95% CI 0.03-1.98). However, they did not find a difference in the risk of term preeclampsia (OR 0.26, 95%CI 0.03–1.98; p = 0.19) or gestational hypertension (OR 1.23, 95% CI 0.63–2.43; p = 0.55). (9) In contrast, another retrospective cohort study of Preaubert *et al.* observed high rates of gestational hypertension and preeclampsia, but similar comparing the double gamete donation and OD group. (10)

Pregnancy of the partner

Taking the risks of OD into account, the consideration of achieving a pregnancy of the partner might be in favour. However, the partner has an impaired kidney function (clearance of 65-70 ml/min) with a dysplastic left kidney and high blood pressure. In addition, achieving a pregnancy would be her first pregnancy. Nulliparous women have an increased risk of developing preeclampsia (OR 2.91; 95% CI 1.28-6.61). (11) Furthermore, patients with chronic kidney disease have a higher chance of developing preeclampsia (OR 10.36; 95% CI 6.28-17.09) and are more likely to have preterm birth, intra uterine growth retardation and a caesarean section. (12) Because of these risk factors we refrained from achieving a pregnancy of the partner.

Artificial insemination with donor sperm

We discussed the possibility of artificial insemination with donor sperm, which is also correlated to an increased risk of preeclampsia. (8) Though this procedure clearly ignores the idea of a joint biological contribution in shared lesbian motherhood, it offers a less complicated and risky procedure. (13) In addition, the patient and her partner stated in later discussions that they would have chosen this alternative primarily, if they were sufficiently informed about the risks of OD pregnancy. For artificial insemination, sperm from the previous or from a new donor could be used. Earlier studies demonstrate that a previous, uncomplicated pregnancy protects against the development of preeclampsia, but that this protective effect disappears with a new partner. (14) The risk of preeclampsia will therefore be lower when the sperm of the previous donor is used.

Eventually, the patient and her partner decided for artificial insemination with sperm of the previous donor. The pregnancy was uncomplicated with a normal blood pressure, prophylactic use of acetylsalicylic acid until 36 weeks of gestation (15-18), and a maximum protein/creatinine ratio of 7.5 mg/mmol. A vaginal delivery went uneventful, three years after her first delivery, and the patient gave birth to a healthy male infant of 3090 grams at 39 weeks and 6 days gestation.

DISCUSSION

To our knowledge, this is the first case report that describes a complication in pregnancy after shared lesbian motherhood. Previous literature discusses mostly the ethical questions related to shared lesbian motherhood. Bodri *et al.* recently described the outcome of 121 lesbian couples that applied to shared lesbian motherhood. (19) In this retrospective study however, the main outcome was clinical pregnancy rate and live birth rate; premature delivery, low birth weight (<2500gr) and caesarean section were the only pregnancy complications described in this cohort. As mentioned, an OD pregnancy, which is the performed ART in shared lesbian motherhood, has a higher risk of developing complications and in particular hypertensive complications. (3-5, 20)

Considering double gamete donation, previous studies are inconsistent in their results. (9, 10) Nevertheless, in case of shared lesbian motherhood, consultation on the risks of possible pregnancy complications is very important, since the couple has a choice to opt for another way of ART, namely artificial insemination with donor sperm. This case report points out shared lesbian motherhood with a complicated pregnancy as a valuable example, in which the decision of OD through ROPA possibly would have been different if the couple was counseled in more detail. Therefore, we aim to emphasize the importance of specialized preconception counseling in shared lesbian motherhood, and any other OD pregnancy. Not only the risks of the IVF procedure should be discussed, but also the risks for pregnancy complications after OD, in particular hypertensive complications. A summary of our preconception counseling advises concerning OD is mentioned in Table 1.

Table 1. Contents of specialized preconception counseling concerning the prevention of hypertensive complications in an oocyte donation pregnancy.

To discuss	Action
Care in a specialized pre-conception consultation	Record the medical history. Give general preconception advise. Support lifestyle improvement.
Use of medication	If necessary, convert to medication that can be used during pregnancy: Stop ACE inhibitors and angiotensin II receptor blockers; Consider stopping calcium channel blockers and diuretics; If necessary, start with methyldopa and/or beta blockers.
Regulation of blood pressure	Measure the blood pressure. In case of hypertension, refer to the general practitioner (systolic ≥140 mmHg).
Possible alternative conception methods	If there are possibilities, weigh the risks of the different treatments.
Risks of developing hypertensive complications in case of oocyte donation pregnancy	Recommend a healthy lifestyle to prevent hypertensive complications. Advise to use low dose aspirin for the prevention of preeclampsia (15-17), despite the low level of evidence for OD pregnancies in particular (18).

LEARNING POINTS/TAKE HOME MESSAGES

- Couples who intend to achieve pregnancy through OD need to be informed in detail, not only about the success rate of the procedure.
- Specialized preconception counseling is advised in which the risks for pregnancy complications, the risks for the gestational carrier and the fetus should be discussed.
- Given the high risk of pregnancy complications, especially hypertensive complications, counseling of an OD pregnancy by a professional obstetrician is recommended.
- A summary of our preconception counseling advises concerning OD is mentioned in Table 1.

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