Case report

Recovery of second trimester pre-eclampsia after fetal reduction of a triplet

Jeske M bij de Weg,¹ Christianne J de Groot,¹ Eva Pajkrt,² Marjon A de Boer¹

¹Obstetrics and Gynaecology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands
²Obstetrics and Gynaecology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands

Correspondence to

Prof Dr Christianne J de Groot,
 cdegroot@me.com

Accepted 27 August 2019

SUMMARY

Women with a multiple pregnancy are at increased risk of developing hypertensive disorders of pregnancy. We describe a case of a dichorionic triamniotic triplet pregnancy complicated by severe hypertension, proteinuria and maternal symptoms, fitting with the diagnosis of pre-eclampsia, apart from the early gestational age of only 16 weeks. After reduction of the monochorionic pair, the disease resolved and pre-eclampsia was diagnosed again at 30 weeks of gestation, resulting in a delivery on maternal indication at 33 weeks of gestation. In a review of the literature, we found six papers including eight cases on multifetal pregnancy reduction on maternal indication. Multifetal pregnancy reduction resulted in a prolongation of pregnancy of two to 21 weeks and may be considered in extreme early onset pre-eclampsia in dichorionic multiple pregnancies.

BACKGROUND

Pre-eclampsia is a common hypertensive disorder of pregnancy. The cause of pre-eclampsia is not completely elucidated yet, but it is thought that abnormal placentation contributes to its onset.¹ Pre-eclampsia is a progressive disorder that can only be cured by delivery of the placenta. Multiple pregnancy and advanced maternal age are among the risk factors for pre-eclampsia.

When counselling women about the perinatal and maternal outcome in a triplet pregnancy, fetal reduction should be considered. In trichorionic triplet pregnancies, reduction to a twin pregnancy was shown to prolong pregnancy by average of three weeks, but the effect on neonatal survival was limited.² In dichorionic triamniotic triplets, reduction to a singleton pregnancy prolonged median gestational age at birth, but did not have an effect on neonatal survival.³ In a retrospective cohort, elective reduction in triplet pregnancies decreased the prevalence of pre-eclampsia compared with ongoing triplets or spontaneously reduced triplets.⁴ Moreover, it has been suggested that in case of early onset pre-eclampsia, fetal reduction may benefit the mother and result in good pregnancy outcome. The aim of this case report is to add new knowledge to the limited amount of available cases on multifetal pregnancy reduction on maternal indication and to present a review of the literature.

CASE PRESENTATION

A half Caucasian and half black pregnant woman aged 40 years presented to our tertiary centre,

Amsterdam UMC, location VUmc Amsterdam, in her first pregnancy at 16 weeks of gestation with complaints of peripheral oedema, transitory headache and nausea. She recently moved to the Netherlands, and was pregnant of a dichorionic triamniotic triplet after in vitro fertilisation after a double embryo transfer. Her general medical history and first antenatal pregnancy controls abroad were uneventful, with a blood pressure of 120/80 mmHg. She was prescribed low dose aspirin, prophylactic low-molecular-weight heparin, corticosteroids and natural progesterone vaginally by her gynaecologist abroad. Family history was positive for pregnancy-induced hypertension (sister).

INVESTIGATIONS

At admission she was alert, had high blood pressure (160/95 mmHg) and her 24-hour urine specimen contained 0.44 g of protein. The laboratory showed elevated liver enzymes: alanine amino transaminase 72 U/L (<34 U/L) and lactate dehydrogenase 271 U/L (<247 U/L). Other laboratory results were normal (table 1). Fetal ultrasound showed growth restriction of one fetus of the monochorionic couple (head circumference (HC) p0.2, abdominal circumference (AC) p0.1 and femur length (FL) p0.8) with an elevated pulsatility index of the umbilical artery (PI 2.48). The second fetus of the monochorionic couple also showed some abnormal measurements (HC p7, AC p88, FL p1) with normal Doppler (PI 1.36). The third fetus showed normal growth and Doppler.

DIFFERENTIAL DIAGNOSIS

The findings of complaints of headache, hypertension and proteinuria resulted in the diagnosis of pre-eclampsia, although by definition it was too early for this diagnosis. Furthermore, a fetal growth restriction of the monochorionic couple in a triplet was diagnosed. Due to the early onset pre-eclampsia, we considered a pre-existent autoimmune disease, in particular systemic lupus erythematosus. This was investigated by a rheumatologist and rejected.

TREATMENT

The patient was admitted to our hospital and given antihypertensive medication (methyldopa 250 mg three times a day). After one day, she clinically deteriorated with increasing complaints of chest pain and dyspnoea. Because of the extreme early pregnancy and the severity of the maternal disease with

© BMJ Publishing Group Limited 2019. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: bij de Weg JM, de Groot CJ, Pajkrt E, et al. *BMJ Case Rep* 2019;**12**:e227667. doi:10.1136/bcr-2018-227667

Table 1 Laboratory results before and after multifetal pregnancy reduction

	Day of admission (GA 16+0)	Day of reduction (GA 16+3)	Day before discharge (GA 17+4)	During visit outpatient clinic (GA 27+5)	Day of readmission (GA 30+4)	Week after readmission (GA 31+4)	Day of delivery (GA 33+6)
Blood pressure (mmHg)	160/95	140/90	130/80	140/85	150/90	132/88	150/95
Haemoglobin (mmol/L) Ref 6.10–8.67 mmol/L	7.2	8.1	6.0	7.0	6.8	6.9	6.5
Thrombocyte ($\times 10^9/L$) Ref 145–352 ($\times 10^9/L$)	159	76	192	157	111	114	88
Creatinine ($\mu\text{mol/L}$) Ref 46–89 $\mu\text{mol/L}$	67	65	60	N/A	79	80	100
ALAT (U/L) Ref 8–40 U/L	72	436	87	N/A	14	13	72
LD (U/L) Ref 162–367 U/L	271	505	270	279	N/A	300	342
Proteinuria (g in 24-hour specimen) Ref <0.224 g in 24-hour specimen	0.44	0.64	0.44	0.18	1.60	1.87	2.23

ALAT, alanine amino transaminase; GA, gestational age in weeks; LD, lactate dehydrogenase; N/A, not available due to haemolysis of blood sample; Ref, reference ranges.¹⁵

increased risk of maternal morbidity and neonatal morbidity and mortality, she and her partner were counselled about termination of pregnancy on maternal indication. In addition, they were counselled about fetal reduction of the monochorionic couple resulting in a singleton pregnancy, thus reducing placental load and possibly improving her clinical condition of pre-eclampsia.^{5–8} She and her husband opted for the reduction of the monochorionic couple of the triplet which was performed at 16 weeks and 3 days of gestation by intracardiac infusion of potassium chloride in one of the monochorionic twins after which both fetuses deceased.

OUTCOME AND FOLLOW-UP

The day of the fetal reduction, maternal symptoms, including dyspnoea and chest pain, were more severe. A day later, her symptoms improved and both blood pressure (120/70 mmHg) and laboratory parameters including proteinuria and thrombocytes normalised (table 1). She remained hospitalised for 12 days. After discharge the patient was followed up in the outpatient clinic at least once a week until 30 weeks and 4 days of gestation when peripheral oedema and proteinuria recurred

(1.22 g in 24-hour specimen) and she was readmitted. After progression of complaints of chest pain and dyspnoea, rising blood pressure (160/90 mmHg) with indication for magnesium sulfate and increasingly abnormal laboratory parameters (table 1), and after receiving corticosteroids, she delivered at 33 weeks and 6 days by caesarean section on maternal indication. A son of 1960 g (26th percentile), Apgar scores 9/10, was born. She recovered uneventful and was discharged three days after the caesarean section. At six weeks postpartum visit, her blood pressure was normal (130/85 mmHg) with nifedipine 30 mg twice a day. At 12 weeks post partum, her blood pressure was 125/90 mmHg still using nifedipine 30 mg twice a day. We advised the patient to visit her general practitioner for blood pressure control and assessment of her antihypertensive medication.

DISCUSSION

We described a case of a primigravid woman aged 40 years with a triplet pregnancy complicated by extreme early pre-eclampsia (16 weeks of gestation). After reduction of the monochorionic twin resulting in a singleton pregnancy, the symptoms of

Table 2 Review of the literature

Reference (first author)	Number of cases	Characteristics	GA at PE	GA at reduction	GA at birth	Interval
Audibert <i>et al</i> ⁹	1	32 years, nulliparous, dichorionic twin, natural conception, discordant growth	28w0d	32w0d	38w0d	6w0d
Delaby <i>et al</i> ¹⁰	1	30 years, G1P0, dichorionic twin, natural conception	28w0d, Ballantyne's syndrome	28w4d	31w5d	3w1d
Fuchs <i>et al</i> ¹¹	1	22 years, nulliparous, dichorionic twin, natural conception, 19w0d discordant growth	31w0d	31w0d	36w0d	5w0d
Heyborne <i>et al</i> ¹²	3	46 years, G2P0, dichorionic twin, donor oocyte, discordant growth	26w0d	26w3d	Term	>10 w
		37 years, G2P0, trichorionic triplet, spontaneous reduction to dichorionic twin in first trimester, donor oocyte, discordant growth	24w6d	24w6d	34w4d	9w5d
		45 years, G2P1, dichorionic twin, IVF	16w0d, Ballantyne's syndrome	16w0d	Term	>21 w
Okby <i>et al</i> ¹³	1	26 years, G4P2, dichorionic twin, natural conception	23w3d	23w4d	27w1d	3w4d
Yu <i>et al</i> ¹⁴	1	24 years, G2P0, dichorionic twin, natural conception, 20w0d discordant growth	26w0d	27w4d	29w0d delivery stillborn, 29w5d delivery healthy neonate	2w1d

GA, gestational age; IVF, in vitro fertilisation; PE, pre-eclampsia.

pre-eclampsia resolved for 14 weeks. At the gestational age of 30 weeks, pre-eclampsia recurred and the pregnancy was terminated on maternal indication at 33 weeks of gestation.

Most reports present cases of reduction on fetal indication. A few cases described lessening or resolution of pre-eclampsia after intrauterine fetal death of one fetus in a multiple pregnancy complicated by pre-eclampsia.^{5–8} We performed a literature search on recovery of pre-eclampsia after multifetal pregnancy reduction, of which after selection on title and abstract remained six full-text paper with a total of eight cases^{9–14} (table 2). All cases of reduction were twin pregnancies, of which one case was in origin a trichorionic triplet with a spontaneous reduction to twins in the first trimester. Pre-eclampsia was described in six cases and Ballantyne's syndrome (fetal hydrops resulting in symptoms of pre-eclampsia) in two cases. In all cases, the fetal reduction was for the benefit of the surviving fetus. Resolution of maternal disease after fetal death was described, although terminating the whole pregnancy would have been more safe. In most cases, delivery could be postponed with recurrence of the pre-eclampsia. The improvement of pre-eclampsia after reduction described in all cases supports the hypothesis that in multiple pregnancies complicated by pre-eclampsia fetal reduction could reduce disease severity, and delivery can be postponed. In our case, the time between the fetal deaths and delivery was over 17 weeks, an interval that only has been described once in a case of Ballantyne's syndrome.¹²

In conclusion, multifetal pregnancy reduction in case of severe pre-eclampsia before viability can establish a long interval between reduction and delivery, which could bridge the gap to viability. Although termination of the whole pregnancy is still the safest treatment of severe hypertension in pregnancy, especially

in cases with extreme early onset. Decision making and counseling should be with multidisciplinary approach including perinatologist and neonatologist in a tertiary centre.

Contributors CJdeG and MAdB were involved in the care and counseling of the patient. Thereby, they conceived and supervised this case report and review of the literature. EP performed procedure of the fetal reduction. JMbdW performed the review of the literature and wrote the manuscript. All authors contributed to the final manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Brosens I, Pijnenborg R, Vercruysse L, *et al.* The "Great Obstetrical Syndromes" are associated with disorders of deep placentation. *Am J Obstet Gynecol* 2011;204:193–201.
- 2 van de Mheen L, Everwijn SM, Knapen MF, *et al.* The effectiveness of multifetal pregnancy reduction in trichorionic triplet gestation. *Am J Obstet Gynecol* 2014;211:536.e1–536.e6.
- 3 van de Mheen L, Everwijn SMP, Haak MC, *et al.* Outcome of multifetal pregnancy reduction in women with a dichorionic triamniotic triplet pregnancy to a singleton pregnancy: A retrospective nationwide cohort study. *Fetal Diagn Ther* 2016;40:94–9.
- 4 Okayay E, Altunyurt S, Soysal D, *et al.* A comparative study of obstetric outcomes in electively or spontaneously reduced triplet pregnancies. *Arch Gynecol Obstet* 2014;290:177–84.
- 5 Hagay ZI, Levy R, Zalel Y, *et al.* Single fetal demise in twin gestation resulting in the resolution of severe pre-eclampsia. *Eur J Obstet Gynecol Reprod Biol* 1994;56:137–8.
- 6 de Boer MA, van Huissteling JC, van Roosmalen J. [Foeto-foetal conflict of interests in multiple pregnancies with severe discordant growth; ethical dilemmas]. *Ned Tijdschr Geneesk* 2005;149:1369–72.
- 7 Narasimhulu DM, Karakash S, Rankin L, *et al.* Resolution of superimposed pre-eclampsia, and improvement in umbilical artery flow in a surviving twin after intrauterine demise of its co-twin. *J Obstet Gynaecol Res* 2015;41:1473–7.
- 8 Sarhanis P, Pugh DH. Resolution of pre-eclampsia following intrauterine death of one twin. *Br J Obstet Gynaecol* 1992;99:159–60.
- 9 Audibert F, Salomon LJ, Castaigne-Meary V, *et al.* Selective termination of a twin pregnancy as a treatment of severe pre-eclampsia. *BJOG* 2003;110:68–9.
- 10 Delaby B, Lanta-Delmas S, Gondry J. Reversal of Ballantyne's syndrome by selective fetal termination in a twin pregnancy. *J Gynecol Obst Bio R* 2008;37:88–92.
- 11 Fuchs F, Zaki D, Morin F, *et al.* Resolution of HELLP syndrome after selective fetocide for trisomy 21 in discordant twins - A case report. *J Obstet Gynaecol* 2016;36:663–4.
- 12 Heyborne KD, Porreco RP. Selective fetocide reverses preeclampsia in discordant twins. *Am J Obstet Gynecol* 2004;191:477–80.
- 13 Okby R, Mazor M, Erez O, *et al.* Reversal of mirror syndrome after selective fetocide of a hydropic fetus in a dichorionic diamniotic twin pregnancy. *J Ultrasound Med* 2015;34:351–3.
- 14 Yu H, Sun W, Yao Q, *et al.* Selective termination in discordant twin pregnancy with early onset preeclampsia: case report. *Clin Exp Obstet Gynecol* 2015;42:696–7.
- 15 Steegers EAP, Thomas DMG, ThM DB, *et al.* Klinisch-chemische referentiewaarden in de zwangerschap. *Elsevier/Bungen* 1999.

Learning points

- In multiple pregnancies, pre-eclampsia can occur early in second trimester.
- Multifetal pregnancy reduction might resolve pre-eclampsia by decreasing placental mass.
- The effect of multifetal pregnancy reduction might be related to abnormal placentation.
- Multifetal pregnancy reduction in case of severe pre-eclampsia before viability can establish a long interval between reduction and delivery, which could bridge the gap to viability.

Copyright 2019 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <https://www.bmj.com/company/products-services/rights-and-licensing/permissions/>
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

Customer Service

If you have any further queries about your subscription, please contact our customer services team on +44 (0) 207111 1105 or via email at support@bmj.com.

Visit casereports.bmj.com for more articles like this and to become a Fellow