## A complicated IVF twin pregnancy

Susan Bewley1, Philippa Moth and Yacoub Khalaf

Guy's and St Thomas' NHS Foundation Trust—Women's Services, 10th floor North Wing, St Thomas' Hospital, Westminster Bridge Rd, London SE1 7EH, UK 

Correspondence address. Tel: | GROC | Fax: | GROC | E-mail:Susan.bewley@ GROC |

Sir,

To illuminate the current debates about multiple embryo transfer, we report a case of a woman who survived massive second-trimester haemorrhage but whose pregnancy was further complicated by intrauterine growth restriction, Caesarean section, premature delivery and resultant cerebral palsy of one twin.

A 29-year-old white hairdresser with twin pregnancy following double embryo transfer had massive bleeding at 20 weeks gestation. First Hb was 5.7 g/dl and she was resuscitated with fluids, blood, fresh frozen plasma and cryoprecipitate. She accepted that pre-viability hysterotomy and emergency termination might be required but wanted to continue the pregnancy. She continued to have intermittent painless bleeding (250–1200 mls/episode) until 24 weeks and was transfused repeatedly. The total estimated blood loss was 18 1 and 27 units blood were given. At 28 weeks, twin 2 had growth restriction, oligohydramnios and reverse end-diastolic flow in the umbilical artery. In view of the risks of death and long-term handicap, conservative management (anticipating intrauterine death of twin 2) and delivery (worsening prematurity outcomes for twin 1) were discussed. After steroids, the babies were delivered by Caesarean section weighing 1240 g and 740 g. Histology confirmed dichorionic diamniotic placenta with no retroplacental clot or infarcts. The babies were discharged after 2 months in hospital. Twin 1 has confirmed cerebral palsy.

Mother's description

I really cannot remember most of the things we talked to the doctors about before the treatment. I just wanted to go ahead and try and have a baby. If they had warned us of what was going to happen I would not have believed them. I was happy to have two embryos back. The night we called the ambulance I thought my babies were going to die. The bleeding was very heavy and wouldn't stop ... The doctors told me that I had bled so much that in order to save my life they may have to take the babies out of my womb to stop the bleeding. I desperately wanted to keep my babies. I received bags and bags of blood. I was so scared, I thought I might die. The nightmare continued for days and days. I kept thinking I had finally stopped bleeding and then I would bleed heavily again ... When the scan showed that one of the babies was not growing, I remember being told that if the babies were not born, then the small baby would die inside me. If the doctors delivered the babies now the bigger one may suffer. I couldn't bear the thought of the smaller baby dying inside me and so it was agreed that the doctors would do a Caesarean. The babies were on the unit for a long time but eventually they were discharged. The little one is well, the bigger one is stiff and makes jerky movements all the time. This experience has made me feel guilty and sad. If someone had tried to sit me down before we started the process, I would never have believed it was all possible. I am sure I will never have any children ever again.

Discussion

We have not found a report of such massive second trimester haemorrhage resulting in two live births. Both placenta praevia and placental abruption are increased in multiple pregnancy (MP). Abruption of twin 2's placenta cannot be excluded though bleeding was presumed to come from twin 1's placenta. Thus the developmental delay may have been antenatal rather than postnatal.

In IVF, the challenge is to achieve a high pregnancy rate with minimal adverse outcomes (El-Toukhy et al., 2006). Despite the publications demonstrating that MP can be reduced by limiting multiple embryo transfer (Gerris et al., 2002; Hamberger et al., 2005; Khalaf et al., 2008), little has been done to impose restrictions in the UK. In Belgium single embryo transfer is mandatory in first cycles in young patients. In Sweden MP has been reduced <5% with single embryo transfer (Karlstrom and Bergh, 2007). Women <30 years with more than four good morphology embryos on day 3 have a good prognosis in their first cycle, but are also at high risk of MP. Here, selective single embryo transfer could have provided a good chance of pregnancy with reduced likelihood of MP, but was not offered. Cryopreservation of any additional embryos could significantly raise the cumulative odds of a live birth (Martikainen et al., 2001). Failure to implement the UK National Institute of Clinical Excellence (NICE, 2004) guideline recommending local provider funding for three IVF cycles in women <39 years has meant that clinicians and patients are reluctant to offer and accept single embryo transfer, respectively. The vast majority of patients fund their own treatment or have only one cycle funded by the National Health Service (NHS). In Australia, where access to IVF is unlimited, or Belgium, where up to six cycles are state funded, a single embryo transfer policy has been easier to implement. The HFEA consulted (HFEA, 2007) and has established a National Strategy Multiple Births Stakeholder Group to advise on its stated aim to reduce the MP rate <10% within 3 years. It may be a false economy for the NHS to only offer one treatment cycle.

Freestanding assisted conception units may lack a full appreciation of the impact of their practices. Some even argue that MP is not a serious complication (van Wely et al., 2006). Some patients regard twins as a positive outcome (Scotland et al., 2007) and will tolerate any risk, but consent is only legally valid if patients are competent, have relevant information and are not acting under duress. It is arguable how freely decisions can be made if an infertile couple is desperate. Limited funding (personal or NHS) inevitably impacts decision-making.

This extreme case demonstrates the full panoply of severely morbid, and potentially fatal, consequences of MP to both mother and babies (Braude, 2006; Kilby et al., 2006). The first reported IVT-related death was associated with twins (Bewley and Wright, 1991), and IVF technologies are now cited in the UK Confidential Enquiry into Maternal Deaths (CEMACH, 2007). As doctors' professional responsibility is to 'first of all, do no harm', they cannot be indifferent to MP and must consider singletons the ideal outcome of treatment. If pregnancy rates were equal, it would surely become unethical, in most cases, to perform multiple rather than single embryo transfer.

Authors' Role

All authors contributed to writing up the case.

Acknowledgment

We thank the patient (whose written permission was obtained).

© The Author 2010. Published by Oxford University Press on behalf of the European Society of Human Reproduction and Embryology. All rights reserved. For Permissions, please email: journals.permissions@oxfordjournals.org

## References

- Bewley S, Wright JT (1991) Maternal death associated with ovum donated twin pregnancy. Hum Reprod 6:898–899. Abstract/FREE Full Text
- 2. Braude P (2006) One Child at a Time. Reducing Multiple Births after IVF. Report of the Expert Group on Multiple Births after IVF, <a href="http://www.hfea.gov.uk/docs/MBSET">http://www.hfea.gov.uk/docs/MBSET</a> report Final Dec 06.pdf. Search Google Scholar
- CEMACH (2007) Saving Mother's Lives. Confidential Enquiry into Maternal Deaths 2003–2005.
- El-Toukhy T, Khalaf Y, Braude P (2006) IVF results: optimize not maximize. Am J Obstet Gynecol 194:322–331. CrossRefMedlineWeb of Science
- Gerris J, De Neubourg D, Mangelschots K, Van Royen E, Vercruyssen M, Barudy-Vasquez J, Valkenburg M, Ryckaert G (2002) Elective single day 3 embryo transfer halves the twinning rate without decrease in the ongoing pregnancy rate of an IVF/ICSI programme. Hum Reprod 17:2626–2631.
   Abstract/FREE Full Text
- 6. Hamberger L, Hardarson T, Nygren KG (2005) Avoidance of multiple pregnancy by use of single embryo transfer. Minerva Ginecol 57:15–19. Medline
- HFEA (2007) The Best Possible Start to Life: A Consultation Document on Multiple Births after IVF, http://www.hfea.gov.uk/docs/The\_best\_possible\_start\_to\_life\_HFEA\_public\_consultation\_paper\_April\_2007.pdf.
- 8. Karlstrom PO, Bergh C (2007) Reducing the number of embryos transferred in Sweden-impact on delivery and multiple birth rates. Hum Reprod 22:2202–2207.

  Abstract/FREE Full Text
- Khalaf Y, El-Toukhy T, Coomarasamy A, Kamal A, Bolton V, Braude P (2008)Selective single blastocyst transfer reduces the multiple pregnancy rate and increases pregnancy rates: a pre- and postintervention study. BJOG 115:385–90.

- 10. Kilby M, Baker P, Critchley H, Field D (2006) Multiple Pregnancy (RCOG Press). Search Google Scholar
- 11. Martikainen H, Tiitinen A, Tomás C, Tapanainen J, Orava M, Tuomivaara L, Vilska S,Hydén-Granskog C, Hovatta O, Finnish ET Study Group (2001) One versus two embryo transfer after IVF and ICSI: a randomized study. Hum Reprod 16:1900–1903. Abstract/FREE Full Text
- $12. \qquad \text{National Institute of Clinical Excellence (2004)} \\ \underline{\text{http://www.nice.org.uk/nicemedia/pdf/CG011fullguideline.pdf.2004.}}$
- 13. Scotland G, McNamee P, Peddie V, Bhattacharya S (2007) Safety versus success in elective single embryo transfer: Women's preferences for outcomes of in vitro fertilisation. BJOG 114:977–983.
- 14. van Wely W, Twisk M, Mol B, van der Veen F (2006) Is twin pregnancy necessarily an adverse outcome of assisted reproductive technologies? Hum Reprod 21:2736–2738. Abstract/FREE Full Text