CEOG Clinical and Experimental Obstetrics & Gynecology

A normal baby is possible despite twins following a single embryo transfer even if one twin is genetically defective

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Summary

Purpose: To demonstrate that it is important to consider all possibilities when confronted with a decision to terminate a pregnancy because it is likely to be chromosomally abnormal. *Materials and Methods:* A cell free DNA test was performed on a woman with dichorionic diamniotic twins that followed the transfer of a single embryo. *Results:* The cell free DNA test was consistent with trisomy 21. Two perinatologists favored identical twins and thus suggested termination since both twins would be trisomy 21 and the couple did not want to raise a child with Down's syndrome. Our group suggested the possibility that these were fraternal twins with one occurring from natural conception. We suggested to forego termination by D&E but to undergo an amniocentesis at 16 weeks. One twin had obvious cardiac abnormalities by ultrasound and this one was reduced while amniocentesis with karyotype was performed on fetus 2. The results showed a normal male. *Conclusions:* One should consider all possibilities before suggesting termination of a very desired pregnancy. This woman had also been advised by other specialists in reproductive endocrinology that conception with her own oocytes (as did occur here) was not possible and she should consider donor oocytes based on her marked diminished oocyte reserve.

Key words: Selective reduction; Single embryo transfer; Dichorionic diamniotic twins; Down's syndrome; Normal baby; Cell free DNA test.

Introduction

Occasionally a physician is faced with a tough decision and may seek the opinion of another colleague or a specialist with more knowledge or experience. Sometimes one can search the literature for precedents. It is always better to evaluate a large series, but for unusual circumstances, one may need to rely on case reports of similar circumstances.

The present case report is described in the title and unfortunately there was no uniformity of opinion among three consulted specialists. In this circumstance, the patient must hear all opinions and make the final decision as to which one makes the most sense to her or best suits her personal needs, but also her personal fears.

Case Report

A 35-year-old woman with a one-year of primary infertility was advised by her first reproductive endocrinologist/infertility specialist that she will require donor oocyte to conceive because her day 3 serum FSH was 28 mIU/ml and her anti-Müllerian hormone level was extremely low at < 0.16 ng/ml (lab states levels > 1.06 ng/ml associated with improved odds for live births and higher antral follicle count). In contrast, she was advised by our group that, especially based on her relatively young age that her prognosis for conception and a live baby was fairly good, that she probably would not need more than one or two embryos.

In her one and only IVF cycle her day 3 FSH was 28 mIU/ml, with a serum estradiol (E2) of 31.7 pg/ml on day 3. With 150 IU of FSH/LH from day 5 with one antral follicle on the left of 11 mm and two pre-antral follicles of < two mm on the right, she attained one mature follicle on the left ovary (18 mm, serum E2: 243) when 10,000 units hCG was given. She had one metaphase II oocyte retrieved. Fertilization was achieved through conventional oocyte insemination. A single six-cell embryo with no fragmentation was transferred on day 3. She conceived that cycle. Her first serum beta hCG level was obtained 15 days from oocyte retrieval and was 299 (mIU/ml). The level was slightly higher than expected four days later (1753) and increased to 5,497 three days later (appropriate) but higher than expected seven days later at 36,014.

The patient was made aware that in our experience, too high of an hCG level even that early can be associated with trisomy 21 (Down's syndrome). At the time that her serum beta hCG level was 5,497, she demonstrated on ultrasound a single eight-mm gestational sac consistent with 5.3 weeks (appropriate). The yolk sac measured 2×2×2 mm. One week later however, two sacs were observed with one measuring 15 mm (consistent with 6.3 weeks) but the sac size of the second one was at ten mm consistent with 5.6 weeks. The crown rump length of number 1 was five mm (6.18 weeks) and was three mm (5.75 weeks) for number 2. The yolk sac for both was 3×3×3 mm and the heart rate for number 1 was 111 bpm and 103 bpm for number 2 fetus. The patient consulted a perinatologist who recommend a cell free DNA test for non-invasive chromosome evaluation since the couple did not want to raise a child with Down's syndrome but did not want to lose this precious complication by a more invasive determination of aneuploidy. The two possibilities to explain the dichorionic diamniotic twins was a cleavage early after the embryo transfer or a pregnancy from a

Revised manuscript accepted for publication September 10, 2015

natural conception from a follicle that developed even after the oocyte retrieval.

An ultrasound performed eight weeks from oocyte retrieval showed on fetus 1 (heart rate 168 bpm, a crown rump length of 27.5 mm (nine weeks and four days) and fetus 2 32 mm (ten weeks and one day). The gestational sac diameter for number 1 was 32.8 mm (eight weeks and five days) and for number 2 was 39.4 (nine weeks and six days).

The cell free DNA test concluded that at least one fetus had trisomy 21. Her perinatologist favored that these were identical twins and suggested a termination by D&E. A second perinatologist similarly suggested termination. They re-consulted our group and it was this author's opinion that she ovulated after the transfer and conceived the second pregnancy naturally. The basis of this opinion was the rarity of cleavages this late to begin with let alone being dichorionic fetuses. Another deciding factor was that we published a previous case report of two embryos seemingly by size 11 days apart and producing live twins [1]. Thus a previous precedent was present [1]. Thus our opinion was to treat with "careful vigilance and benign neglect" and hope that if there is only one with Down's syndrome, it may spontaneously abort. Though one did not spontaneously die, the smaller one with level II ultrasound after the first trimester showed a serious cardiac anomaly. Based on this observation selective reduction was performed and amniocentesis on the larger gestational sac showed a normal male. However, because the cells were not adequate, three different perinatologists were concerned about trisomy 21 mosaicism in "an identical twin" and still suggested termination. The couple again asked our opinion. Again, we suggested to take a chance with delivery because we believed that the "normal" male karyotype further supported our contention that they were fraternal twins. We argued that with her very severe oocyte reserve depletion and the need for IVF because of tubal factor we could guarantee another successful pregnancy if we did IVF again. They decided to heed our advise and delivered a perfectly normal healthy boy.

Discussion

Though top specialists in their field, because the three perinatologists were not aware that delayed implantation can occur a second time despite a first implantation, they favored an extremely rare dizygotic diamniotic identical twins, even after embryo transfer of one embryo with size discrepancies, allowing them to favor the opinion that another very rare event occurred, i.e., mosaicism in the second fetus with the normal cells growing out following amniocentesis. Furthermore their lack of knowledge that conception could still occur even after retrieval of one oocyte led the perinatologists to suggest termination of what turned out to be a perfectly normal fetus. Hopefully the publication of this case report and the establishment of another precedent may help another physician/couple make the proper decision of pregnancy termination or not.

References

[1] Check J.H., Chase J.S., Nowroozi K., Goldsmith G., Dietterich C.: "Evidence that differences in sizes of fraternal twins may originate from early gestation - a case report". *Int. J. Fertil.*, 1992, *37*, 165.

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