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Successful pregnancy following in vitro fertilization-embryo transfer in a woman with diminished oocyte reserve despite a slow rising beta human chorionic gonadotropin level

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Summary

Purpose: To present another rare case of a live pregnancy despite an inappropriate rising serum beta hCG level. *Materials and Methods:* A woman with diminished oocyte reserve had an in vitro fertilization (IVF) cycle, so the precise day of ovulation was known. *Results:* Despite an inappropriate doubling time for the serum beta-hCG level and a crown rump length sac size discrepancy (small sac), an apparently healthy fetus with no apparent anomalies has passed the second trimester. *Conclusions:* Despite the risk of ectopic pregnancies with slow rising hCG levels, and the generally very low chance of a successful viable pregnancy, one may need to not be too quick to terminate the pregnancy with methotrexate.

Key words: Slow rising beta-hCG; Viable pregnancy; Small gestational sac; Diminished oocyte reserve; Methotrexate.

Introduction

A slow-rising serum hCG level almost invariably is associated with subsequent fetal demise even if viability is still seen at eight weeks [1]. The authors of that publication carefully monitored many pregnancies over the next nine years and finally found an exception to the rule [2]. Subsequently a second exception was found [3].

Presented herein is the third exception to the rule by the same authors, but the first one conceived with in vitro fertilization-embryo transfer (IVF-ET) and diminished oocyte reserve.

Case Report

A 33-year-old woman with primary infertility of one-year duration had her first in vitro fertilization (IVF) cycle cancelled at another facility because of poor response after ten days of standard dosage of gonadotropins for controlled ovarian hyperstimulation. She was subsequently found to have a low anti-Müllerian hormone level of 0.25 ng/ml.

A second cycle was attempted with clomiphene first, followed by recombinant follicle stimulating hormone (FSH) and human menopausal gonadotropin. Five oocytes were retrieved, three fertilized, and two cleaved to day 3 and were transferred. There was no pregnancy.

She conceived on her third IVF attempt, but first IVF-ET cycle at the present institution, using a mild FSH stimulation protocol [3-5]. She was started with 150 IU FSH on day 6 and low dosage hCG (10 IU) was added when cetrorelix 250 mg was added.

Her peak serum estradiol reached 888 pg/ml when 10,000 IU hCG was given. There were four oocytes retrieved all of which were metaphase II, two fertilized and on day three two eight-cell embryos of good quality were transferred. She conceived.

Her first beta-hCG level was 48 mIU/ml obtained 14 days after oocyte retrieval. The hCG level failed to double in two days. In fact, it only reached 96 four days later. She was told that this pregnancy was probably going to end in a miscarriage. Her next hCG beta subunit taken two days later also failed to rise appropriately (only 155 mIU/ml). Five days later it doubled appropriately from the previous 155 to 1,180 mIU/ml. However, the 1,180 mIU/ml level was consistent with 21-22 days from conception but taken 25 days from conception and should have been ~5,000 mIU/ml. The next beta-hCG did not double appropriately and only rose to 3,058 mIU/ml four days later so should have been 4,500 mIU/ml. Actually from conception the level should have been between 8,000 mIU/ml.

Her first ultrasound taken 18 days from conception should have shown six weeks, but the crown rump length of three mm was consistent with 5.75 weeks, but the sac measuring seven mm was consistent with five weeks. A repeat ultrasound taken one week later showed appropriate growth of the fetal pole (crown-rump length eight mm consistent with 6.75 weeks but the sac lagged further behind (12 mm consistent with 5.86 weeks). She was advised of the poor prognosis when a sac lags one week or more behind [6]. When based on day of retrieval she should have been 7.14 weeks, her sac average was 12 mm, consistent with 5.86 weeks. She was started on azithromycin. The fetal heart rate was 136. One week later there was appropriate growth of the crown-rump length, now consistent with 7.9 weeks. The gestational sac

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grew just short of one week getting to an average of 19 mm consistent with 6.22 weeks. The heart rate was 171. Two weeks later the fetal pole crown rump length was perfect at 10.14 weeks and the sac enlarged to 42 mm consistent with 9.34 weeks and the heart rate was 182. At her final ultrasound, staying on azithromycin, her sac and crown rump length finally matched and was consistent with the conception date with 57 mm for sac average (12.12 weeks) and 61 mm for crown rump length (consistent with 11.9 weeks). The heart rate was 176. She did have the panorama non-invasive prenatal test which suggested no evidence of increased risk of trisomy-21, trisomy 18, trisomy 13, or monosomy. She had a successful full-term delivery.

Discussion

Knowledge of case reports that are the exception to the rule helps prevent making clinical mistakes. In this case, the poor odds of this conception turning out to be a good pregnancy with the initial failure to show adequate rise of the serial beta-hCG levels, one common choice would have been to terminate the pregnancy with methotrexate to prevent a possible ruptured ectopic pregnancy.

It is well known that a slow-rising sera beta-hCG level is a common presentation of tubal pregnancies. Of course a slow rising beta-hCG level is also commonly found in women with intrauterine pregnancies that will eventually spontaneously abort. The two recent exceptions to the rule with live pregnancy cases with slow rising beta-hCG levels helped influence the decision not to terminate the pregnancy, but proceed with careful vigilance and benign neglect.

The preciousness of the pregnancy, a woman with diminished oocyte reserve on her third expensive IVF cycle, should be given the benefit of the doubt that, though unlikely, this could become the exception to the rule and result in a live delivery. Besides, the slow rising beta-hCG levels, another poor prognostic factor was the crown rump length/sac size discrepancy [6]. Though we have never evaluated treatment with azithromycin when the gestational sac is small in a controlled manner to publish our data, or have a case that convincingly suggests that this treatment can improve the prognosis, since instituting this policy we at least seem to have a much lower pregnancy loss rate when the sac seems one week or more behind the age based on crown-rump length.

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