Case Reports in Women's Health 21 (2019) e00096

Contents lists available at ScienceDirect

Case Reports in Women's Health

journal homepage: www.elsevier.com/locate/crwh

A case report of an abnormal trend in hCG levels in a pregnancy complicated by ovarian hyperstimulation syndrome

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ARTICLE INFO

Article history:
Received 15 January 2019
Accepted 22 January 2019

Keywords:
OHSS
hCG
Early pregnancy
Abnormal trend

ABSTRACT

Objective: To present a case of abnormally trending hCG levels due to ovarian hyperstimulation syndrome (OHSS) and to portray the obscurities of this commonly used method for tracking early pregnancies.
Design: Case report.
Setting: Outpatient ART facility.
Patient: A patient who received controlled ovarian hyperstimulation in an ART cycle.
Intervention: Supportive care.
Main outcome measure: hCG level.
Result: The hCG levels in this patient with OHSS trended in an abnormal fashion, suggesting a failing or ectopic pregnancy, but the patient had a normal intrauterine fetus.
Conclusion: hCG levels may be falsely low in pregnancies complicated by OHSS.

1. Introduction

Human chorionic gonadotropin (hCG), a hormone produced by trophoblast cells surrounding a growing embryo, is used as a biomarker of early pregnancy. Tracking the changes in serum hCG levels over time can also give insight into the health and viability of a pregnancy. According to the American College of Obstetricians and Gynecologists [1], the expected rate of increase in 48 h is 49% for an initial hCG value under 1500 mIU/mL. According to Barnhart et al., a viable intrauterine pregnancy should see a minimum increase of 53% in hCG levels in that range. Although different minimum thresholds for hCG rise in normal pregnancies have been proposed, there is a significant range of indeterminate values. At levels below this minimum threshold, the pregnancy may be considered non-viable: either failing or extrauterine, leading to recommended physician counseling toward diagnostic and therapeutic intervention [2].

Human chorionic gonadotropin is uniquely produced by the syncytiotrophoblast cells of a gestational fetus or embryo and can be detected in the maternal serum as early as eight days after ovulation, just after the time of embryo implantation. The rate of rise of hCG in IVF pregnancies is similar to that in spontaneous conceptions [3]. In a study by Chung et al. of 391 IVF pregnancies that ended in live births, the average slope of the hCG rise for viable pregnancies was 0.403, indicating a predicted increase of 50% in one day and 124% in two days. In that study, the smallest rise in two days that ended in a live birth was 30%. Conversely, a study by Barnhart et al., based on a retrospective cohort of 287 patients, showed that the lowest rise in hCG level in 48 h in which a viable pregnancy ensued was 53%.

Standard rates of hCG rise in patients with ovarian hyperstimulation syndrome (OHSS) have not been well assessed and may be different than in standard patients. OHSS is a complication of controlled ovarian stimulation; it leads to dynamic fluid shifts from the intravascular compartment to the extravascular one. In a 2017 case-control study by Choux et al. assessing hCG levels of women with OHSS, the data implied that maternal hCG values at different time points of the pregnancy were lower in OHSS than in controls, essentially stating that a pregnancy complicated by OHSS will have a lower hCG value than a non-OHSS pregnancy at the same gestational age. The study concluded that differences in hCG levels and kinetics should be taken into account in patients with OHSS [4]. However, no rate of increase was clearly defined in this study.

2. Materials and Methods

We present a patient suffering from OHSS after gonadotropin ovarian stimulation and intrauterine insemination (IUI) with an abnormal trend in hCG levels, which was significantly below the expected rate of rise yet ultimately resulted in a viable intrauterine pregnancy. We obtained consent from the patient for publishing this article.

This patient presented to our ART clinic complaining of an inability to conceive for 12 months. She was twenty-four years old and diagnosed with primary infertility and polycystic ovary syndrome (PCOS). She was initially prescribed clomiphene citrate for ovulation induction

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https://doi.org/10.1016/j.crwh.2019.e00096

but failed to ovulate; she was then transitioned to gonadotropin stimulation for ovulation induction.

3. Results

During the treatment cycle she had a maximum estradiol level of 2176 pg/mL and had two follicles >16 mm noted on pelvic sonogram. Ovulation was triggered with 250 μg of recombinant hCG, and she underwent IUI 36 h later. Five days after insemination, she complained of nausea, anorexia, dyspnea, and bloating. On physical exam abdominal distention, tachypnea and a fluid wave were noted; on ultrasound, she was noted to have hyper-stimulated ovaries measuring 113 × 91mm on the left and 87 × 95mm on the right, in addition to pelvic ascites. Her lab values revealed evidence of hemoconcentration with a hematocrit of 45 mg/dL, hyponatremia with a sodium level of 132 mmol/L, and leukocytosis with a WBC of 19×10^3/μL. Her hCG level of 62 mIU/mL rose over 48 h to 76 mIU/mL: a mere 23% increase, which is well below the expected rate for viability. Initially, she was managed conservatively with intravenous hydration and supportive care as she declined a culdocentesis for symptomatic relief. She was subsequently managed as an outpatient with clinical and laboratory assessment of her hypovolemia and hemoconcentration. While her symptoms of OHSS slowly resolved, her hCG levels continued to increase sub-optimally over the next 48 h (by 29%, from 72 to 98 mIU/mL). While there was concern about a non-viable or ectopic pregnancy, the patient remained stable and was managed conservatively with observation. Her symptoms continued to improve, and hCG assessment six days later showed a reassuring increase to 665 mIU/mL, followed by 4476 mIU/mL seven days later. An ultrasound scan that day confirmed an intrauterine pregnancy, and 14 days later the patient had an hCG level $>40 \times 10^3$ mIU/mL and sonographic evidence of a normal-appearing eight-week intrauterine pregnancy with a well-formed fetus and a fetal heart rate of 165.

4. Discussion

Dynamic fluid shifts from the intravascular compartment to the interstitium are a hallmark of OHSS. In this specific case, such fluid shifts were the likely cause of the suboptimal, or “abnormal”, hCG rise in an otherwise normal pregnancy. With OHSS, there is extravasation of fluid into tissue and cavities, causing intravascular hemoconcentration. This patient, for instance, had notable ascites and lab values demonstrating hemoconcentration. Subsequently, during the recovery phase, that extravascular fluid shifts back into the intravascular compartment, creating in effect hemodilution. This hemodilution creates the falsely low hCG rise, while it is in essence an artifact of a rapid increase in intravascular fluid. Once the fluid shift resolved, though, the hCG level rose in a more “normal” fashion.

This case report demonstrates that the standard hCG curve does not always rise in a “normal” fashion. There are many factors that contribute to the increase in level, and providers should not deem a pregnancy abnormal until all factors have been considered. We believe that OHSS should be an important clinical factor for providers to consider when measuring β-hCG levels in early pregnancy. Moreover, providers should not expeditiously recommend diagnostic or treatment modalities in these situations if it is a desired pregnancy.

The limitations of this report include its limited reproducibility and its retrospective nature. The strengths include its concordance with other reports in the literature and its relevance to ART. The case was managed appropriately from both the providers' and the patient's perspective, and this case can be generalized to a larger population: those with OHSS and pregnancies of unknown location.

Contributors

Ariel Benor wrote the paper.
Richard Grazi contributed data and managed the patient.
David Kulak analyzed and interpreted the data.

Conflict of interest

The authors have no conflict of interest in regards to this paper. There was no financial arrangement for any of the work done here. This paper was not presented at any meeting or conference.

Funding

No funding was sought or secured in relation to this case report.

Patient consent

Obtained.

Provenance and peer review

This case report was peer reviewed.

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