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CASE REPORT

Spontaneous Late Onset OHSS in Singleton Pregnancy in 2nd Trimester: A Rare Case

Patil Hampanagouda N. · Roy Rajib · Pal Raja · Roychowdhury Joydeb

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About the Author

Hampanagouda N. Patil passed senior secondary school from JNV ALMATTI, Bijapur, Karnataka, in 2004, CBSE; passed MBBS from Sri B.M.Patil Medical College Bijapur, RGUHS, Bangalore, in 2010; and MS PGT (OBG) at ESI-PGIMSR, Joka, AI Quota. He has presented free papers at BOGSCON 2013 & AICOG 2014. His ongoing thesis work is about Hysteroscopic evaluation in patients with abnormal uterine bleeding and its correlation with histopathology. He has attended BOGSCON 2013 & 2014, and AICOG 2014 Patna. His special interests include gynaec oncology, hysteroscopy, and laparoscopy

Introduction

Ovarian hyperstimulation syndrome (OHSS) is a potentially life-threatening complication of pharmacological ovarian stimulation. It is seen in approximately 2 % of all IVF cycles. The prevalence of moderate to severe OHSS ranges from 1 to 10 % in major IVF programs. Severe forms complicate 1 % of IVF cycles and are characterized by massive ovarian enlargement together with a fluid shift into extravascular compartments responsible for the development of ascites, sometimes pleural and/or pericardial effusion, hypovolemia, oliguria, and hydroelectrolytic disorders. In the most marked cases, thromboembolic phenomena may occur as a result of hemoconcentration and coagulation disturbances (Hollemaert et al. [1]).

Spontaneous ovarian hyperstimulation (spontaneous OHSS) is extremely rare in naturally conceived pregnancies. OHSS in the absence of exogenous gonadotropins is very rare, and only a few cases have been reported in the literature. Spontaneous OHSS likely to occur at 8–14 weeks of gestation, while iatrogenic OHSS usually occurs earlier at 3–8 weeks of gestation [2]. Human chorionic gonadotropin (hCG) is thought to play a crucial role in the development of the syndrome. Severe forms are indeed restricted to cycles with exogenous hCG to induce ovulation or as luteal phase support or with endogenous pregnancy-derived hCG (Delbaere et al. [3]).

Here, we report a rare case of spontaneous 2nd trimester OHSS in 22-year-old primigravida.

Patil H. N. · Roy R., Assistant Professor · Pal R., Assistant Professor · Roychowdhury J., Professor & HOD
Dept of Obst & Gynae, ESI-PGIMSR & ESIC Medical College & Hospitals, Joka, Kolkata, India

Roychowdhury J. (✉), Professor & HOD
BE-177, sector-1, Salt Lake, Kolkata 700064, West Bengal, India
e-mail: rcjoydeb@gmail.com

Case Report

22-year-old primigravida, married for 2 years, conceived spontaneously, presented at 16 week with complaints of mild to moderate intermittent lower abdominal pain for 15 days, progressive swelling of abdomen along with nausea, and vomiting for 2 days. There was no history of fever. On admission her pulse rate was 112/min, BP-124/80 mmHg with mild pallor; her abdomen was distended due to ascites with mild diffuse tenderness. On further examination, uterus was found 16–18 weeks in size. Initial investigations revealed Hb-9 g%, TLC-12000, PCV-27 %, platelets-3.6 lakh, serum albumin-3.3 g%, K^+-7.6 mmol/L, Ca-7.0 mmol/L, TSH-5.49 μIU, T3-145 ng/dL, T4-7.4 μg/dL, AST-81U, and ALT-50U. USG showed single live fetus of 15 weeks, with bilateral enlarged multicystic ovaries (14 × 15 cm), largest cyst (5 × 4 cm). On assay of tumor markers, serum βHCG level showed very high level-547672 miu and CA125-262.9U, and AFP was 48.32U. USG-guided aspiration of cyst sent for cytology was negative for malignancy, cell count was 180/ml. Ascitic fluid was also sent for cytology which showed cell count-400/mL, negative for malignancy, sugar-98 mg/dL, protein-3.3 g/dL, LDH-158U, and ADA-15U. Patient was managed conservatively with IV fluids, IV human albumin in infusion pump of 40–60 mg/day, antibiotics, input output charting along with serial monitoring of βhCG, TLC, Electrolytes, protein, urea, creatinine. The beta hCG level persistently remained very high with the following serial values done every 48 h: 547672, 664943, 491256, 494986, and 468922 mIU/mL. Abdominal paracentesis was done to aspirate 800–1000 ml of ascitic fluid on 3 occasions to reduce the patients' discomfort. Her ascites was improving and she remained hemodynamically stable. But on day 14 of her admission, she started experiencing severe epigastric pain with progressive distension of abdomen. Abdominal paracentesis was done which showed hemorrhagic fluid. Emergency laparotomy was done same day suspecting ruptured cyst. During surgery, 4 L of hemorrhagic peritoneal fluid was drained, and bilateral multicystic ovaries with multiple cyst ruptures were seen. Bilateral ovarian cystectomy was done without disturbing pregnancy (Figs. 1, 2).

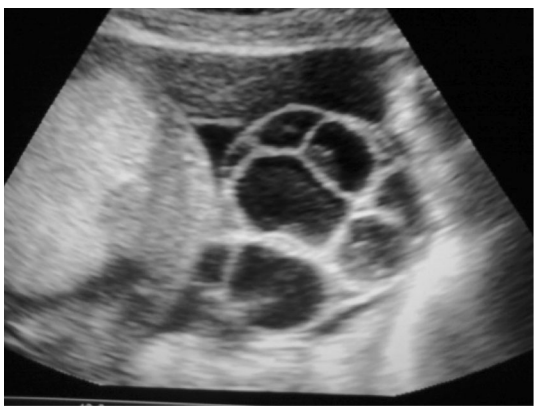

Fig. 1 USG picture of enlarged multicystic ovaries

Residual ovarian tissue was preserved on both sides. HPE showed hemorrhagic benign follicular cysts without any evidence of malignancy. Postoperative recovery was uneventful with falling βhCG titers. β-hCG titer dropped to 146328 mIU/mL on the 2nd postoperative day, and then it came down to 75567 ImIU/mL after 1 week. On 2nd postoperative day, USG was done which showed live fetus of 17 weeks, with ascites, bulky placenta, and no adnexal mass. But after 2 weeks, the patient stopped perceiving fetal movement and USG showed intrauterine death of fetus. Medical termination of pregnancy was done. No gross fetal anomaly was seen; birth weight of the fetus was 500 g. Placental histopathology showed hemorrhagic and fibrinoid necrosis with degenerated chorionic villi. Patient was followed up with weekly βhCG, showing rapidly falling trend like 2254, 261.5, 151.2, 88, 4, and 0.1 mIU/mL. The patient is under follow up till date with normal beat hCG value, and she has started regular periods with no evidence of iatrogenic ovarian failure. The prospect of recurrence of similar event of severe OHSS in the subsequent pregnancy is being adequately assessed and discussed with the patient.

Discussion

OHSS is a systemic disease mediated by vasoactive products released from hyperstimulated ovaries and is considered to be an iatrogenic complication of ovulation induction therapy. However, OHSS may rarely be associated with spontaneous ovulatory cycles as in this case.

The etiopathogenesis of spontaneous OHSS is not studied well. Spontaneous OHSS can occur both in pregnant and non-pregnant women. De Leener et al. [4] classified spontaneous OHSS syndrome into three types based on clinical presentation and FSH receptor mutation. Type I is associated with the mutated FSH receptor, and this type may cause recurrent spontaneous OHSS. Type II is secondary to high levels of hCG as in hydatiform mole and multiple gestation, and is the most frequent one. Type III is related to hypothyroidism.

Hyperstimulated ovaries release a number of vasoactive mediators under the influence of hCG. These include vascular endothelial growth factor and several pro-inflammatory cytokines that interact to produce the characteristic pathophysiology of OHSS. This is marked by increased capillary permeability, leakage of fluid from the vasculature, third space fluid accumulation, and intravascular dehydration [5].

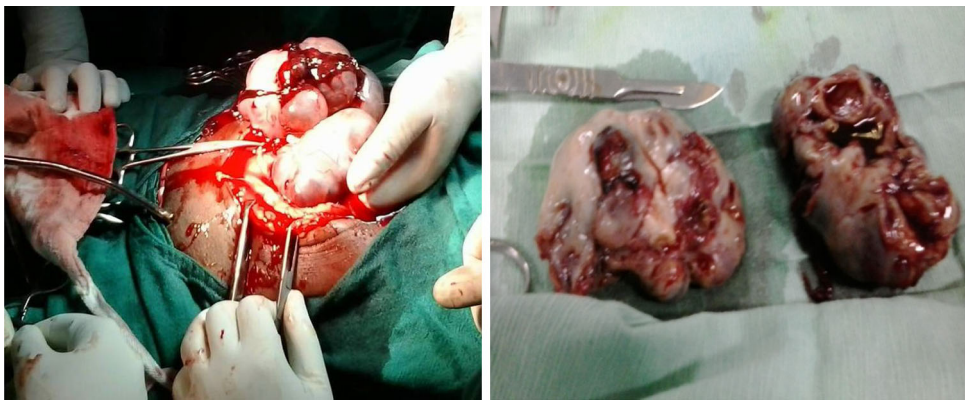

Fig. 2 Laparotomy showing enlarged hemorrhagic cysts ruptured and removed

The recent identifications of mutations in the FSH receptor gene, which display an increased sensitivity to hCG, are considered responsible for the development of spontaneous ovarian hyperstimulation syndrome (OHSS) and provide the molecular basis for the physiopathology of spontaneous OHSS.

In the iatrogenic form, the follicular recruitment and enlargement occur during ovarian stimulation with exogenous FSH, while in the spontaneous form, the follicular recruitment occurs later through the stimulation of the FSH receptor by pregnancy-derived hCG. In both forms, massive luteinization of enlarged stimulated ovaries ensues, inducing the release of vasoactive mediators, leading to the development of the symptoms of OHSS. In our case also, it was a singleton spontaneous euthyroid pregnancy, and therefore hyperstimulation of FSH receptor to endogenous hCG can only explain this hyperstimulation. But this patient presented at 15 weeks of pregnancy when normally spontaneous OHSS should not be present because of normally declining hCG in singleton pregnancy. In our case, hCG level remained very high even at 15–16 weeks of pregnancy and the source of hCG appeared to be from the hyperstimulated luteinised ovaries since after bilateral cystectomy hCG level started coming down even before the fetal demise that happened after 2 weeks of surgery. The subsequent features of OHSS disappeared gradually and the patient recovered. The cause of fetal death is unfortunate and may be due to OHSS-related hemoconcentration, electrolyte disorders, or due to postsurgical effect or may be due to sudden decline of hCG before placenta is functionally well-formed. The hemorrage and placental infarcts on histology can explain the placental disorder as a result of OHSS in this case. There are reports in the literature where live birth was possible. Olatunbosun et al. [6] in 1996 reported a case of spontaneous OHSS in a patient with polycystic ovarian disease, who experienced severe spontaneous OHSS in four consecutive singleton pregnancies and achieved live births in two of the pregnancies. But OHSS was managed by medical support, and no surgical intervention was required in those cases. Therefore, surgery is always avoided unless there are complications like massive pleural or pericardial effusion where thoracocentesis are essential or laparotomy may be required in cases of rupture of hyperstimulated cysts as happened in our case.

Conclusion

During spontaneous OHSS, the 'initial' corpus luteum related to the pregnancy is not responsible for the development of the OHSS symptomatology. The formation of 'secondary' multiple corpora lutea, or at least of a critical mass of luteinized granulosa cells, could induce a massive release of vasoactive mediators leading to the development of the syndrome.

Conflict of interest The authors declare that there is no conflict of interest.

Compliance with Ethical Requirements The undersigned authors declare that the article is original, neither the article nor part of it is under consideration for publication anywhere else and has not been previously published anywhere. We have declared all vested interests. The article, if published, shall be the property of the journal, and we surrendered all rights to the editor. We agree to provide the latest follow up of cases prior to the publications of case reports when requested. The authors also had taken ethical clearance and permission from the patient before surrendering the manuscript.

References

1. Hollemaert S, Wautrecht J, Capel P, et al. Thrombosis associated with ovarian hyperstimulation syndrome in a carrier of the factor V Leiden mutation. Thromb Haemost. 1996;76:275–6.
2. Smits G, Olatunbosun O, Delbaere A, et al. Ovarian hyperstimulation syndrome due to a mutation in the follicle-stimulating hormone receptor. N Engl J Med. 2003;349:760–6.
3. Delbaere A, Bergmann PJM, Gervy-Decoster C, et al. Angiotensin II immunoreactivity is elevated in ascites during severe ovarian hyperstimulation syndrome: implications for pathophysiology and clinical management. Fertil Steril. 1994;62:731–7.

4. De Leener A, Montanelli L, Van Durme J, et al. Presence and absence of follicle-stimulating hormone receptor mutations provide some insights into spontaneous ovarian hyperstimulation syndrome physiopathology. J Clin Endocrinol Metab. 2006;91:555–62.
5. Alper MM, Smith LP, Sills ES. Ovarian hyperstimulation syndrome: current views on pathophysiology, risk factors, prevention, and management. J Exp Clin Assist Reprod. 2009;6:3.
6. Olatunbosun OA, Gilliland B, Brydon LA, et al. Spontaneous ovarian hyperstimulation syndrome in four consecutive pregnancies. Clin Exp Obstet Gynecol. 1996;23:127–32.