



Case Report

A Case of Ovarian Hyperstimulation Syndrome in Two Consecutive Naturally Conceived Pregnancies

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ABSTRACT

Ovarian hyperstimulation syndrome (OHSS) is a rare, life-threatening complication of assisted fertility treatment. Rarely, overstimulation of the ovaries can occur in naturally conceived pregnancies. However, limited data are available in the literature. A 24-year-old woman, in her first pregnancy, conceived naturally and presented with moderate abdominal pain at 6 weeks of gestation (POG). She was diagnosed with mild OHSS. However, at 10 weeks, she developed a right-sided twisted ovary and an incomplete miscarriage. Nine months later, she conceived again naturally, which was also complicated by OHSS; hence, she received pregnancy care and OHSS management. Her pregnancy was further complicated by preeclampsia. At 35 weeks of POG due to moderate OHSS and preeclampsia, a baby was delivered via caesarean delivery. This reports the early development of OHSS in two consecutive naturally conceived pregnancies. One was complicated with ovarian torsion and spontaneous first-trimester miscarriage, while the second pregnancy ended up with a healthy baby despite the complications of preeclampsia and preterm delivery. Continued surveillance for complications and carrying out timely interventions were crucial components in the management of this case.

Keywords: Follicle-stimulating hormone, Natural conception, Ovarian hyperstimulation syndrome, Pregnancy

INTRODUCTION

Ovarian hyperstimulation syndrome (OHSS) is a rare, life-threatening complication of assisted fertility treatment. In assisted fertility treatment, pharmacological agents are used to stimulate the ovaries to increase the number of oocytes and subsequently increase the number of embryos. Some women who undergo assisted fertility treatment may develop overstimulation of the ovaries. Overstimulated ovaries induce specific pathophysiological changes which lead to the syndrome of ovarian hyperstimulation.^[1]

OHSS commonly occurs due to the overstimulation of ovaries by ovulation-inducing agents, such as gonadotropins. Rarely, overstimulation of the ovaries can occur in women who conceived naturally due to the increased sensitivity of follicle-stimulating hormone (FSH) receptors to human chorionic gonadotropin (hCG).^[2] Overstimulated ovaries produce vascular endothelial growth factor and several pro-inflammatory mediators, and the excess production of these mediators appears to cause ovarian enlargement and increased vascular permeability. These pathophysiological changes result in an intracellular fluid shift to the third space compartments, which then give rise to the clinical features of OHSS, such as hypovolemia, haemoconcentration, hypercoagulability, ascites and pleural effusion.^[3,4]

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OHSS is associated with significant physical and psychosocial morbidity. There have been several reported deaths due to OHSS during assisted fertility treatment.^[5-7] Based on the severity, the Royal College of Obstetricians and Gynaecologists have proposed clinical, ultrasonographic, haematological and biochemical features to classify OHSS into four categories, namely mild, moderate, severe and critical OHSS.^[8]

The incidence of OHSS is widely varied and predominantly described with fertility treatment. A majority of the patients who undergo assisted fertility treatment develop mild OHSS^[9] which is self-limiting and managed primarily with fluid management and supportive care. Compared to mild OHSS, moderate and severe OHSS are relatively less common and reported to have a combined incidence of 1.1% following *in vitro* fertilisation.^[10] Patients with moderate, severe and critical OHSS need prompt intensive treatment in a specialised setting with multidisciplinary assistance for the management of complications.

Despite a few case reports, there has been limited data in the literature concerning the incidence of the spontaneous onset of OHSS in naturally conceived pregnancies.^[11-13] In this article, we report a case of OHSS that occurred in a pregnant woman who had conceived naturally in the Sri Lankan context.

CASE REPORT

Mrs H is a 24-year-old woman in her first pregnancy, conceived naturally, who presented with moderate abdominal pain and discomfort to the gynaecology inpatient unit at 6 weeks of the period of gestation (POG). She had no history of fertility treatment. Following the admission, she had been thoroughly assessed, and the common causes of abdominal pain, such as ectopic pregnancy, urinary tract infection, pelvic infection and appendicitis, were excluded. Her ultrasound scan of the abdomen and pelvis revealed enlargement of the right ovary (9 cm × 9 cm × 8.5 cm) with multiple thin-walled ovarian cysts. Her left ovary appeared normal, and there was no ultrasonic evidence of ascites. A viable intrauterine pregnancy in a fibroid uterus (7 cm × 5 cm) was noted. Her renal, liver, full blood count and thyroid function tests were normal. She was diagnosed with mild OHSS associated with a naturally conceived pregnancy based on the size of the ovaries; her symptomatology and other investigations were not deranged. She was managed with fluid management and supportive care during the 4-day hospital stay. After initial management, she was discharged and arranged for close follow-up as an outpatient.

At 10 weeks of POG, she was readmitted to the same unit with severe abdominal pain and mild vaginal bleeding and was found to have a non-viable foetus on the ultrasound scan of

the abdomen and pelvis. She was suspected of having a right-sided twisted ovarian cyst and was offered an emergency laparotomy. The right-sided twisted ovarian cyst was confirmed during the surgery. The left ovary and the uterine tube appeared normal. Right-sided salpingo-oophorectomy and myomectomy were performed along with evacuation of retained products of conception. The postoperative period had been uncomplicated. She was discharged on the seventh day following the surgery. The histopathology report revealed no evidence of malignancy, and her follow-up scan showed a normal ovary.

Nine months later, she again presented to the gynaecology outpatient setting with a POG of 5 weeks and 3 days. She had conceived naturally, and the transvaginal scan revealed an intrauterine pregnancy with unknown viability. Furthermore, she was found to have an enlarged left ovary (6.9 cm × 6.7 cm × 6.5 cm) with multiple small simple cysts. Based on the scan findings and clinical features, she was diagnosed with mild OHSS for the second time. She had been carefully followed up in an outpatient setting with continued surveillance for complications. The routine abdominal ultrasound scan at 13 weeks of POG found a healthy ongoing pregnancy; however, the size of the left ovary had been further increased (7.9 cm × 7.3 cm × 6.7 cm), and mild free fluid was noted in the abdomen. Her serum hCG level was compatible with the gestational age. Since she was clinically asymptomatic and did not have features of severe or critical OHSS, she continued to be managed as an outpatient. At 16 weeks of POG, her pregnancy got complicated further with high blood pressure. Her full blood count, renal function and liver functions were normal to rule out end-organ damage and possible preexisting hypertension, and she was commenced on nifedipine.

At 30 weeks and 5 days of POG, she was admitted to the obstetric ward with complaints of abdominal pain and difficulty breathing. She was not in labour on admission. Her blood pressure was normal on admission, and there were no symptoms or signs of preeclampsia. She had been kept as an inpatient under close observation in an obstetrics setting. She was continued on supportive treatment for moderate OHSS together with blood pressure monitoring, preeclampsia screening and regular assessment of foetal well-being. Her blood pressure was 140/100 mmHg on several occasions despite regular treatment with nifedipine 20 mg twice a day. At 35 weeks of POG, her urine albumin became positive. Considering the risk of severe hypertension and proteinuria, considering the hospital logistics and the availability of the facility, a decision was made to deliver her. Her informed consent was taken for an elective caesarean delivery at 35 weeks of POG due to moderate OHSS and preeclampsia. After the completion of dexamethasone, the elective caesarean delivery was performed, and a baby with

a birth weight of 2.26 kg was delivered. The APGAR score on delivery was normal; however, the baby was admitted to the special baby care unit due to prematurity. During the surgery, an enlarged multicystic ovary was noted with free fluids in the peritoneum. Her postpartum period had been uncomplicated. The repeat ultrasound scan of the abdomen at 48 hours of the postpartum period did not show free fluids in the abdomen. The mother was discharged from the hospital on the fourth day following the delivery. Her postpartum follow-up scan revealed an ultrasonically normal ovary.

DISCUSSION

OHSS is a known complication associated with assisted fertility treatment. Spontaneous OHSS in naturally conceived pregnancies has been seldom described in the literature. The above case study highlights the development of OHSS in two consecutive naturally conceived pregnancies in a woman in her mid-twenties. Such case studies are scarce in the literature; therefore, it is important to document this case study. As per the awareness of the authors, this is the first reported case study of OHSS that occurred in a subsequent naturally conceived pregnancy in a woman who has undergone unilateral oophorectomy in the Sri Lankan context.

Vasseur and colleagues in 2003 described a possible mechanism for the development of spontaneous OHSS in naturally conceived pregnancies. They have demonstrated a mutation in the serpentine domain of the FSH receptor that makes the receptor hypersensitive to chorionic gonadotropins, which results in overstimulation of the ovaries.^[14] Therefore, women with this mutant gene can experience recurrent OHSS in subsequent naturally conceived pregnancies. Dassanayake and others have reported a similar case study of a woman who had developed OHSS in two naturally conceived pregnancies in the Sri Lankan context.^[15] In our case subject, the mutant FSH receptor may be one of the possible explanations for her experience of OHSS in both pregnancies. However, due to limited resources, we have not performed genetic studies to confirm such mutations.

In our case study, the patient was diagnosed with mild OHSS at 6 weeks of POG during her naturally conceived first pregnancy and offered supportive care with continued surveillance for complications. Spontaneous OHSS usually develops between 8 and 14 weeks of gestation.^[16] At 10 weeks of POG, she developed a right-sided twisted ovarian cyst, and her pregnancy ended as a first-trimester miscarriage. She had to undergo a right-sided salpingo-oophorectomy as a life-saving therapeutic measure due to ovarian necrosis. Surgical intervention is indicated in patients with OHSS with coincidental problems such as adnexal torsion, ectopic pregnancy or ovarian rupture.^[8] There have been published case reports of performing bilateral oophorectomy for

severe and intractable OHSS.^[17] In our patient, the right-sided salpingo-oophorectomy was performed due to ovarian torsion and subsequent necrosis.

Ovarian torsion commonly occurs in the first trimester or early second trimester of pregnant women with OHSS.^[18] The rate of ovarian torsion in OHSS is widely variable in the literature. According to a retrospective analysis of a nationwide sample in the United States, ovarian torsion developed only in 2.1% of women with OHSS, and 11.5% of them underwent oophorectomy.^[19] In the same study, ovarian torsion is more frequently observed in pregnant patients with OHSS compared to non-pregnant patients with OHSS. Since the majority of cases of OHSS are managed in an outpatient setting, awareness and active monitoring for the risk of ovarian torsion are mandatory, particularly in pregnant women.

Women who undergo unilateral salpingo-oophorectomy for adnexal torsion have an increased risk of subsequent subfertility. In a recent report of 26 patients who underwent unilateral oophorectomy for adnexal torsion, Al-Turki and Haifa found a 53.9% increased risk of infertility in their sample.^[20] However, the patient in our case study had a natural conception for the second time after 9 months following the right-sided salpingo-oophorectomy.

Similar to the first pregnancy, the patient developed a recurrence of OHSS in the second pregnancy during the sixth week of POG. Her remaining left ovary was found to be enlarged, along with mild free fluids in the abdomen, subsequently. The pregnancy got further complicated with the detection of high blood pressure during the second trimester. Despite multiple complications, the pregnancy was continued with careful monitoring of foetal and maternal wellbeing, and in the third trimester, the patient developed preeclampsia that led to an elective preterm delivery at 35 weeks of POG. Data related to late gestational complications of pregnancies with OHSS are limited in the literature. A case-control study of 40 pregnant women with OHSS conducted in France reported that the incidence of pregnancy-induced hypertension and preterm labour was significantly higher in pregnant women with OHSS compared to pregnant women without OHSS.^[21] In the same study, 21.2% of pregnant women with OHSS developed pregnancy-induced hypertension, while 36% of pregnancies ended as preterm labour. In a study conducted on 125 pregnant women with severe OHSS, Hass and colleagues also found a significant increase in the rates of preterm delivery, particularly in singleton pregnancies.^[22] The Royal College of Obstetricians and Gynaecologists recommends treating clinicians be aware of the increased risk of preeclampsia and preterm delivery in women with OHSS, and such women need to be informed about the risks.^[8]

CONCLUSION

OHSS, though typically associated with assisted reproductive technologies, can occur in naturally conceived pregnancies. Our case report highlights the development of OHSS while both pregnancies were conceived spontaneously. The first pregnancy was complicated with ovarian torsion and spontaneous first-trimester miscarriage, while the second pregnancy ended up with a healthy baby despite the complications of preeclampsia and preterm delivery. Continued surveillance for complications and carrying out timely interventions were crucial components in the management to prevent serious complications and mortality.

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