# Large-Volume Paracentesis, up to 27 L, With Adjuvant Vaginal Cabergoline in the Case of Severe Ovarian Hyperstimulation Syndrome with Successful Pregnancy Outcome: A Case Report

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Severe ovarian hyperstimulation syndrome (OHSS) is a potentially life-threatening complication of assisted reproductive technology. Herein, we report the case of an infertile couple, with the husband being azoospermic, who underwent *in-vitro* fertilisation and intracytoplasmic sperm injection at our institute. The woman presented with late OHSS 7 days after embryo transfer. Inpatient management was performed with intensive surveillance. Oral cabergoline was started prophylactically but was replaced by the vaginal route due to intolerance. Transvaginal paracentesis was performed five times over 20 days, and a total of 27 L of ascitic fluid was drained. The patient improved substantially and had a further uneventful pregnancy course. This case report helped us theorise that large-volume paracentesis is safe and efficacious in the management of severe OHSS. In addition, the vaginal route of cabergoline administration is more favourable than the oral route in view of lesser side effects and better patient compliance.

**Keywords:** Cabergoline, ovarian hyperstimulation syndrome, paracentesis

### INTRODUCTION

*O* varian hyperstimulation syndrome (OHSS) is common with gonadotropin therapy used in assisted reproductive technology. The hallmark of OHSS is the fluid shift from intravascular to third space due to increased capillary permeability. In patients with tense ascites, paracentesis is performed to improve the symptoms. The maintenance of intravascular volume and adequate renal perfusion is crucial. Cabergoline is an effective prophylactic agent for the prevention of OHSS in high-risk patients.

## CASE

We, hereby, report the case of a couple with late-onset OHSS, who presented to our fertility clinic with 10 years of primary infertility. Mrs. X, a 36-year-old woman with a body mass index (BMI) of  $29.71 \text{ kg/m}^2$ , had regular menstrual cycles. Her clinical examination was normal. Her hormone profile was normal with day 3 levels as follows: Follicle stimulating hormone (FSH) – 6.35 mIU/mL, LH – 4.70 mIU/mL, anti-mullerian hormone (AMH) – 2.34 ng/mL, estradiol (E2) – 47.11 pg/mL, thyroid stimulating hormone (TSH) – 1.48 mIU/mL and prolactin – 12.56 ng/mL.

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Her ultrasonography (USG) revealed a normal-sized uterus with an antral follicle count of 22.

Her spouse, 37-year-old, was azoospermic with bilateral normal-sized testis and normal karyotype. Intracytoplasmic sperm injection was planned with testicular sperm confirmed using trial testicular sperm aspiration prior to *in-vitro* fertilisation. Long protocol downregulation was started from day 21 of the previous cycle (leuprolide acetate 1 mg s.c. for 10 days). Stimulation was given with recombinant follicle stimulating hormone (rFSH) 150 IU s.c. daily from day 2 to day 10. On day 11 USG, 10 follicles  $\geq$ 10 mm and 8 follicles <10 mm were observed. Thereafter, we replaced rFSH with urinary human menopausal gonadotropin (uHMG) 75 IU from day 11 to day 15. In addition, human chorionic gonadotropin (hCG) trigger

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10,000 IU i.m. was given. On the day of trigger,  $E_2$  was 2160 pg/mL. Eight oocytes were retrieved. Oral cabergoline 0.25 mg daily was started prophylactically from the day of hCG trigger to prevent OHSS in view of the higher number (n=16) of small follicles and polycystic ovaries on basal scan. USG on the day of embryo transfer (ET) revealed mildly enlarged ovaries, with a volume of 95.87 and 91.47 cc in the right and left ovaries, respectively. Two grade-I embryos were transferred on day 3.

One week after ET, the patient returned with complaints of nausea, vomiting, abdominal distension, pain abdomen and mild dyspnoea for the past 3 days. USG suggested an enlarged left ovary of volume 190 cc and a right ovary of volume 98 cc with moderate free fluid in the Pouch of Douglas. The patient was admitted and asked to avoid excess fluid intake. She was haemodynamically stable but had moderate ascites. There was no involvement of the respiratory system. Daily weight and abdominal girth were monitored, as well as input-output monitoring. An investigation of blood parameters revealed haematocrit of 48%, total protein level of 5.7 g/dl and normal liver and kidney function tests. There was no evidence of coagulopathy. These parameters were serially repeated. There was progressive hypoproteinemia. The patient was started on symptomatic analgesics and antiemetics. Human-albumin infusion (albudac - 20%, 100 mL; Zydus Cadila Healthcare Ltd, India) was given repeatedly. She had progressive dyspnoea, abdominal discomfort and tense ascites. USG was suggestive of severe ascites and enlarged ovaries (left and right ovarian volumes - 210 and 120 cc, respectively). Transvaginal paracentesis was performed for symptomatic relief, and 4.5 L of ascitic fluid was drained. Her beta-hCG titre, 2 weeks after ET, was 621 mIU/mL. As a result of recurring ascites and troublesome dyspnoea, transvaginal paracentesis was performed five times over 20 days, and a total of 27 L of ascitic fluid was drained. She required seven albumin infusions. The patient was not tolerating oral cabergoline. She improved after switchover to vaginal cabergoline. USG at 7 weeks confirmed twin viable foetuses. The patient was discharged after 1 month of hospitalisation in good general condition. She was a resident of Bangladesh and took further antenatal care in her country. On telephonic conversation, she communicated to have had an uneventful pregnancy course. She delivered two healthy female babies (birth weight 2.4 and 2.25 kg, respectively) at 36 completed weeks of gestation by an elective caesarean section.

#### DISCUSSION

There is an evolving concept of OHSS-free clinics that aim to eliminate OHSS occurrence by using gonadotropin releasing hormone (GnRH) agonist trigger in the antagonist cycle and simultaneously freezing all embryos.<sup>[1]</sup> In our patient, we went ahead with ET because the patient was asymptomatic;  $E_2$  on the day of trigger was only 2160 pg/mL, and ovaries were not significantly enlarged. She developed late OHSS because of twin pregnancy.

Clinical trials have reported a benefit towards the reduction of OHSS and ascites after oral cabergoline.<sup>[2]</sup> Motta et al. concluded that vaginal cabergoline is a good alternative to oral cabergoline.<sup>[3]</sup> Our patient was not tolerating oral cabergoline, and we observed a significant improvement in emesis and ascites after its vaginal application. There is a paucity in the literature comparing the efficacy of these two routes of administration in OHSS. According to Cochrane review, intravenous albumin administration at the time of oocyte retrieval plays a preventive role in patients at severe risk for OHSS.<sup>[4]</sup> Delvigne and Rozenberg reviewed that the incidence of OHSS in albumin-treated versus -untreated groups was 8.3 and 14.6%, respectively.<sup>[5]</sup> Gokmen et al. observed that both albumin and hydroxyethyl starch might prevent moderate-to-severe OHSS.<sup>[6]</sup> We had administered albumin to reduce the severity of OHSS.

This patient had unremitting symptoms and recurring ascites; therefore, she required multiple ascitic fluid tapping. In symptomatic OHSS with large volume of ascitic fluid on imaging, paracentesis is a logical choice. Paracentesis reduces intra-abdominal pressure in OHSS and causes immediate relief of dyspnoea and renal perfusion. Another mechanism hypothesised is via the elimination of toxic derivatives such as inflammatory substances produced by hyperstimulated ovaries.<sup>[7]</sup> Paracentesis has not been found to have any adverse pregnancy outcome; instead, it increases uterine artery perfusion.<sup>[8]</sup> The patient discussed here was also pregnant and underwent five sittings of transvaginal paracentesis. Ascitic fluid tapping should be performed at a moderate pace while maintaining adequate hydration at the same time. Ozgun et al. reported a case in which they had safely drained a total of 45 L of ascitic fluid and 7.5 L in one course with satisfactory improvement of the patient's condition.<sup>[9]</sup> Similarly, in our patient, we did serial transvaginal paracentesis and removed 27 L of ascitic fluid. The patient tolerated the procedure well. In severe OHSS, large-volume paracentesis and the adjuvant use of vaginal cabergoline is a safe and effective management option.

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#### **Conflicts of interest**

There are no conflicts of interest.

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