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CASE REPORT

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Management of ovarian hyperstimulation syndrome with abdominal compartment syndrome, based on intravesical pressure measurement

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Abstract

There are few reports on abdominal compartment syndrome that are caused by ovarian hyperstimulation syndrome (OHSS). Here, a case of a 29 year old woman is reported in which intravesical pressure measurement was useful in the management of severe OHSS that had been complicated by abdominal compartment syndrome. The patient's urinary output and general condition did not improve after the initial treatment. The woman's intra-abdominal pressure was evaluated indirectly, based on her intravesical pressure, and was found to be significantly elevated. The patient's urinary volume increased after a 14 mm Hg decrease in the intravesical pressure was achieved by the drainage of ascitic fluid. Intravesical pressure measurement was useful in the management of the general condition of this patient with OHSS.

KEYWORDS

abdominal compartment syndrome, disease management, intra-abdominal pressure, intravesical pressure, ovarian hyperstimulation syndrome

1 | INTRODUCTION

Ovarian hyperstimulation syndrome (OHSS) is primarily an iatrogenic disease that is characterized by an exaggerated response to ovulation induction therapy.[1] This iatrogenic complication results from a loss of control of ovarian stimulation and can occur with any agent that is used to induce ovulation.[1–4] Ovarian hyperstimulation syndrome consists of a variety of symptoms and signs, including ovarian enlargement, third-space fluid collection, hemoconcentration, pleural effusion, ascites, and abdominal discomfort subsequent to increased vascular permeability.[1,2,5]

The treatment of OHSS usually requires i.v. fluid management to reduce the volume of ascitic fluid and to reverse hemoconcentration in order to improve the urinary output because a patient's condition depends on the retention of fluid in the third space,[1,2] while i.v. albumin also is used to reverse low serum albumin levels and to maintain urinary output.[1]

It has been reported that the increase in intra-abdominal pressure (IAP) that is associated with OHSS exacerbates its symptoms.[6] It is also known that abdominal compartment syndrome (ACS) may be caused by increased IAP due to severe ascites in emergency care and general surgery settings. Increased pressure in the abdominal cavity can lead to compromised organ perfusion, similar to the compartment syndrome in limbs, which is a potentially life-threatening condition.[7,8] However, there are only a few reports of OHSS that is complicated with ACS.[3,6,9]

Here, a case is reported in which intravesical pressure measurement was useful in the management of a patient who was diagnosed with severe OHSS that was complicated with ACS.

2 | CASE REPORT

A 29 year old nulliparous woman with a history of ovulation disorder was diagnosed as having primary infertility at her first visit. She failed to conceive despite receiving multiple courses of clomiphene citrate. Thus, the ovulation stimulation agent was switched from clomiphene to daily

human menopausal gonadotropin (hMG) (basal luteinizing hormone, follicle-stimulating hormone, etc. were not calculated and the protocol of ovarian stimulation was unknown). An ultrasound examination revealed that her ovaries had enlarged to 6 cm in size (the follicular size and number were unknown and serum E2 was not calculated) after the initiation of hMG therapy. Human chorionic gonadotropin (hCG) (2500 U) then was used to trigger ovulation. On day 4 of hCG treatment, she presented with mild abdominal distention. An ultrasound examination revealed that the ovaries had enlarged to 11.6 cm in size. She was followed up on an outpatient basis due to the presence of mild ascites. On day 14 of hCG therapy, an ultrasound examination revealed no change in the bilaterally enlarged ovaries and an increase in the mild ascites. A pregnancy test was negative at the time. On day 22 of hCG therapy, the patient was admitted to her former hospital with severe abdominal distention and severe leg edema. An ultrasound examination revealed enlarged ovaries (left, 15.2 cm; right, 12.6 cm) and severe ascites. A chest X-ray showed severe pleural effusion. The patient was diagnosed with OHSS based on the clinical picture and the ultrasonographic evidence. A pregnancy test was positive and hypouresis of 155 mL/d was observed. She was therefore transported to Gifu University Hospital, Gifu, Japan.

The woman's height was 166 cm and her body weight was 62.8 kg, which was 15.8 kg heavier than her usual weight. Her blood pressure was 105/77 mm Hg and her pulse rate was 90–100 beats/min. Her oxygen saturation level was 98% on room air and she was not febrile. She had a tender and markedly distended abdomen with prominent shifting dullness. An ultrasound examination revealed enlarged ovaries and severe ascites (Figure 1). She also had edema in the bilateral lower extremities. The initial laboratory results indicated mild hemoconcentration: hemoglobin, 12.6 g/dL; hematocrit, 36.1% (from a baseline hematocrit of 30%); serum creatinine, 0.64 mg/dL; albumin, 2.8 g/dL; and D-dimer, 2.0 μg/mL (Table 1). A chest X-ray film showed severe right pleural effusion (Figure 2).

At the time of her admission (when her symptoms were mild), a 14 Fr Foley catheter was inserted intravesically and a central venous line was inserted to allow rapid initial hydration and to facilitate the strict monitoring of the patient's fluid intake, central venous pressure, and urinary output. Fluids (100–150 mL/h, extracellular fluid) and albumin (5%) were administered i.v. However, the patient's urinary volume did not increase and her central venous pressure did not recover. Furthermore, she began to experience dyspnea and her IAP, which was measured indirectly based on the intravesical pressure, was found to be significantly elevated (25 mm Hg).

Ultrasound-guided paracentesis was performed and 2000 mL of ascitic fluid was drained. Following a 14 mm Hg decrease in intravesical pressure, the patient's urinary volume increased from 20–30 mL/h to ~150 mL/h. Finally, after the draining of 6000 mL of ascitic fluid, the patient's intravesical pressure dropped to 6 mm Hg and her urinary volume was maintained at 100–150 mL/h (Figure 3). Heparin was administered the following day because her laboratory data revealed that her D-dimer level had risen to 3.9 μg/mL; however, a computed tomography scan revealed no thromboembolic event and her hematocrit level remained at 32.8%.

TABLE 1 Changes in the patient's laboratory data

Item	Admission (Day 1)	Day 1	Day 7
White blood cell count (/μL)	11 320.00	10 800.00	12 800.00
Hemoglobin (g/dL)	12.60	10.80	11.30
Hematocrit (%)	36.10	36.10	32.00
Creatinine (mg/dL)	0.64	0.56	0.53
Albumin (g/dL)	2.80	2.60	2.60
D-dimer (μg/mL)	2.00	3.90	3.60

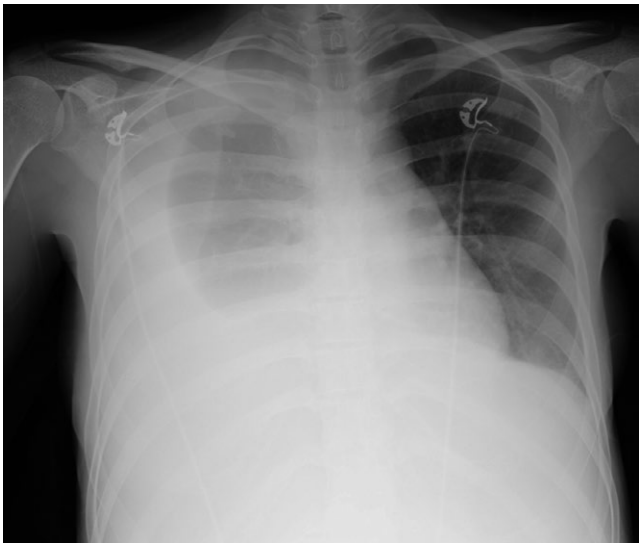

FIGURE 2 Chest X-ray film shows severe right pleural effusion at admission after 23 days of human chorionic gonadotropin administration

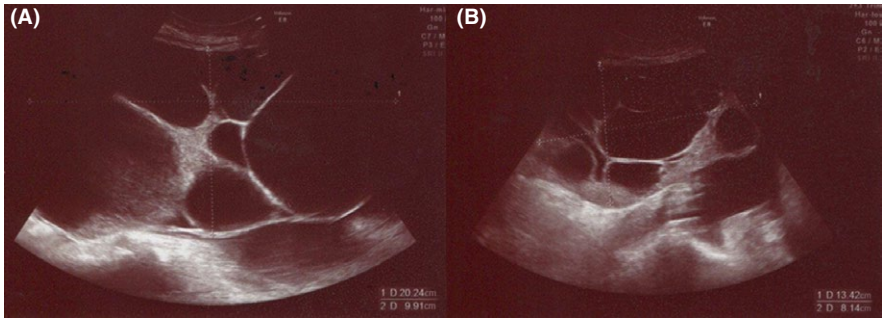

FIGURE 1 Ultrasound findings at admission after 23 days of human chorionic gonadotropin administration. A, The left ovary (20 cm × 10 cm) shows the characteristic features of ovary hyperstimulation syndrome (OHSS). B, The right ovary (13 cm × 8 cm) also shows features of OHSS

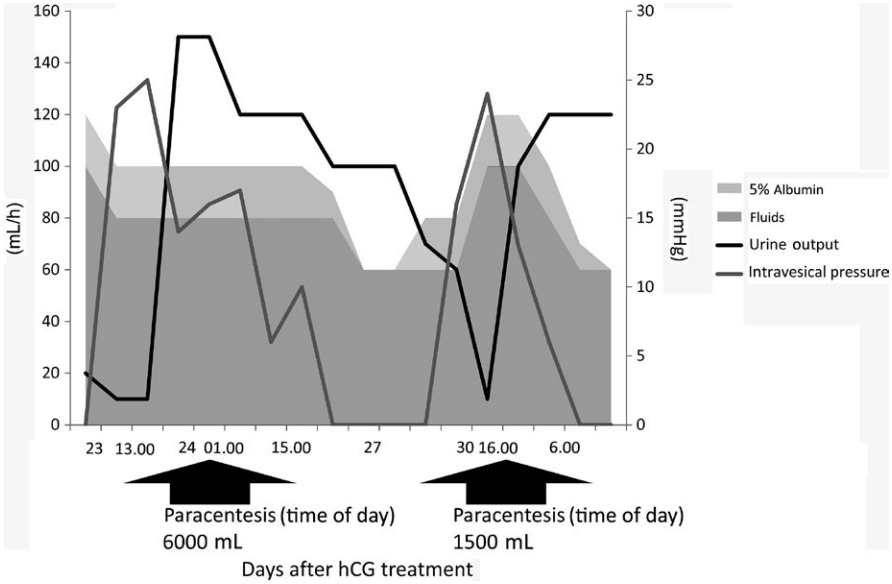

FIGURE 3 Timeline of the patient's urinary output and management during the first 7 days of hospitalization. hCG, human chorionic gonadotropin

Subsequently, the patient's urinary volume progressively decreased to 10 mL/h. On day 7 of hospitalization, the patient's intravesical pressure was again found to be significantly elevated, at 24 mm Hg. A further 1500 mL of ascitic fluid was drained and the patient's urinary volume improved to 120 mL/h, following a 13 mm Hg decrease in intravesical pressure (Figure 3). Her condition improved and a fetal heartbeat was confirmed on day 35 of hCG therapy. The patient was discharged on day 25 of hospitalization.

The patient's ovaries were normally sized at the 18th gestational week. Her condition remained favorable as the pregnancy progressed. The onset of labor occurred at 39 weeks and 3 days of pregnancy and she gave birth via natural vaginal delivery to a girl who weighed 3080 g.

3 | DISCUSSION

Due to the widespread availability and use of assisted fertility techniques, the incidence of OHSS has increased steadily since the first case was reported in 1943.[3] Recently, several treatment modalities, including the administration of gonadotropin-releasing hormone antagonists, have been used to decrease the incidence of moderate OHSS, which is estimated to occur in 0.6%-2.5% of patients who undergo assisted fertility treatment. The severe form occurs in 0.1%-1% of *in vitro* fertilization cycles.[10–14] Ovarian hyperstimulation syndrome is a significant complication in reproductive medicine because the disease is a purely iatrogenic disorder that results from uncontrolled ovarian stimulation due to exogenous means of ovulation induction. In the most severe cases, OHSS is potentially life-threatening as patients can suffer from thrombosis, renal insufficiency, and respiratory failure.[15,16]

Ovarian hyperstimulation syndrome has been reported to cause the overexpression of vascular endothelial growth factor (VEGF) from the ovaries and to promote angiogenesis and vascular hyperpermeability.[1,14] It is also reported that hCG increases VEGF expression in human granulose cells and raises serum VEGF concentrations.[15] Vascular endothelial growth factor is an angiogenic cytokine, which is a potent stimulator of the vascular endothelium and appears to play an integral role in follicular growth, corpus luteum function, and ovarian angiogenesis.[14] Recent studies also indicate that VEGF levels correlate with the severity of OHSS.[1] High intra-ovarian renin angiotensin system activity is another pathophysiological mechanism that has been implicated in OHSS.[14] The ovarian renin angiotensin system is involved in regulating vascular permeability, angiogenesis, endothelial proliferation, and prostaglandin release.[14]

Aboulghar and Mansour reported the first classification of OHSS that combined both laboratory and clinical findings.[17] Although various disease severity classifications have been proposed, OHSS traditionally has been classified as "mild," "moderate," or "severe."[17,18] Severe OHSS, which requires hospitalization, is characterized by the presence of vomiting (sometimes uncontrollable), dyspnea, accumulation of fluid in the third space with hydrothorax, and/or tense ascites (with pain) and evidence of intravascular fluid loss, hypovolemia with hemoconcentration, electrolyte imbalance, oliguria, and/or hepatorenal failure, with an ovary diameter of >12 cm.[17] The patient in the present study was diagnosed with severe OHSS according to that classification. Ovarian hyperstimulation syndrome is also classified, based on the timing of its manifestation, as "early" or "late."[14] Early OHSS occurs within 9 days of hCG treatment, which is used as an ovulatory trigger, and reflects the effect of exogenous hCG.[14] Late OHSS occurs after >10 days of hCG treatment and reflects the effect of endogenous hCG that is being produced by the establishment of pregnancy.[14] In the present case, the patient was considered to have mild OHSS in the early stage of the disorder and that her condition was aggravated at the late stage by the establishment of pregnancy.

The management of severe OHSS is primarily performed via supportive bodily fluid management. This consists of close monitoring of

the volumetric status via a urinary catheter and central venous line because the condition occurs due to the retention of fluid in the third space.[1] Patients with severe OHSS require i.v. fluid for initial hydration. Thereafter, fluid management should be implemented in order to maintain an adequate urinary output and reverse hemoconcentration. If no improvement is seen after the initial treatment, albumin therapy might be effective in treating hypoalbuminemia.[1] However, in the present case, the infusion of albumin did not improve the patient's urinary output. In addition, fluid management was challenging because the hypovolemia was caused by the extravasation of the intravascular fluid. Therefore, the patient's fluid balance was carefully monitored by closely following not only her input and output, but also her changes in weight and central venous pressure. It is generally expected that a patient's urinary volume will increase after the initial treatment with albumin because it is thought that oliguria in patients with OHSS is caused by the decreased renal blood flow that occurs with hypovolemia. However, the patient's hemoconcentration values were not remarkable at the time of hospitalization and improvement was not seen after i.v. fluid hydration and the infusion of albumin. Therefore, the patient's IAP was measured indirectly by evaluating the intravesical pressure. Consequently, her intra-abdominal hypertension was able to be recognized and the patient was diagnosed with ACS. On the basis of these findings, it was considered that the oliguria was caused mainly by compression of the renal veins. Therefore, the compression of the renal veins was relieved by draining the ascitic fluid and the volume of urine increased.

"Abdominal compartment syndrome" is defined as the combination of an IAP of >20 mm Hg and a new organ dysfunction.[8,19] Various organ systems are directly or indirectly influenced by intra-abdominal hypertension. For example, acute liver dysfunction can occur due to liver cell damage, mesenteric ischemia can occur due to a disturbance of mucosal microperfusion, and renal dysfunction can occur as a result of renal vein compression. The normal IAP of 5–7 mm Hg can increase due to various factors, such as abdominal surgery, ileus, intra-abdominal hemorrhage, or ascites (as occurred in the present case).[7,8]

Respiration can be impaired by the elevation of the diaphragm because the increased IAP reduces the functional residual capacity of the lung.[8] Furthermore, preloading of the heart can decrease due to compression of the renal and mesenteric veins. It is reported that oliguria occurs due to renal function disorder at an IAP of 10 mm Hg and that the vascular resistance of the renal vessels increases by ≤500% at IAP values of >20 mm Hg.[8] Furthermore, intravesical measurement has been reported to be the most accurate method for evaluating IAP.[19] In the present case, the patient's intravesical pressure increased to 25 mm Hg at the time of oliguria. The draining of the ascitic fluid resulted in a decrease in the IAP, which allowed the urinary volume to improve and prevented the progress of ACS, thereby avoiding an artificial abortion.

Recently, concentrated ascitic reinfusion therapy has been reported to be an effective method to supplement the albumin that is removed by paracentesis.[20–22] However, this method was not able to be chosen in the present case because the decline in albumin was slight at the time of the paracentesis, the laboratory data were atypical, and paracentesis was urgently required at night.

In conclusion, intravesical measurement was a useful method for monitoring and indirectly evaluating the IAP of a patient with OHSS when the initial care failed.

DISCLOSURES

Conflict of interest: The authors declare no conflict of interest. *Human rights statement and informed consent*: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and its later amendments. Informed consent was obtained from all patients for being included in the study. *Animal rights*: This article does not contain any studies with animal subjects performed by the any of the authors.

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