A Fatal Case of Ovarian Hyperstimulation Syndrome

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ABSTRACT

Aim: This case report is aimed to study an ovum donor, hospitalized with severe ovarian hyperstimulation syndrome (OHSS) and anuria.

Background: Ovarian hyperstimulation syndrome is an iatrogenic complication now on the rise with the increasing use of assisted reproductive technologies and ovulation induction. The syndrome can range from mild symptoms to life-threatening conditions.

Case description: A 30-year-old patient with abdominal distention, anuria, and ultrasonography suggestive of grossly enlarged ovaries. The patient was managed with hemodialysis and multidisciplinary approach until she had an ovarian follicular rupture with hemoperitoneum and had to undergo surgical management.

Conclusion: Patients with high risk for OHSS should be hospitalized and monitored closely when undergoing assisted reproductive methods like intrauterine insemination or ovulation induction. The condition is managed by medical therapy and surgical intervention is required only if the ovarian cysts rupture, undergoes torsion or patient starts debilitating vitally.

Clinical significance: Careful selection of candidates for assisted reproductive technology (ART), close monitoring and prompt management can control the progression of OHSS from mild to critical and can be lifesaving.

Keywords: Assisted reproductive technique, Gonadotropin releasing hormone antagonists and agonists, Ovarian hyperstimulation, Ovum donor.

INTRODUCTION

Incidence of OHSS varies from 0.9 to 1.4%. Multiple enlarged follicular cysts accompanied by increased capillary permeability are classical of OHSS. The increased vascular permeability causes a shift of intravascular fluid to the third compartment space leading to ascites, pleural and pericardial effusion, electrolyte imbalance, and reduced levels of albumin. First described in 1943, the first fatal cases were documented in 1951; mortality rate associated with OHSS is estimated from 1/45,000 to 1/500,000.

CASE REPORT

A 30-year-old female was received in emergency services ward at our tertiary care hospital with complaints of abdominal distention, breathlessness, pain in abdomen for 4 days and anuria for 2 days. She was a habitual ovum donor and had undergone ovulation induction with gonadotropins for 21 days in her last menstrual cycle followed by ultrasound guided vaginal ovum pickup. On day 2 post-ovum donation, patient started experiencing severe pain in abdomen with distention, breathlessness, and oliguria. She was taken to a local hospital where she was treated with analgesics and IV fluids. After 48 hours on worsening of her condition, she was referred to our tertiary care center for the further management.

On examination, bilateral pedal edema was present, pulse was 98 per minute, blood pressure was 120/80 mm Hg, respiratory rate was 36 per minute with decreased air entry on right side, saturation maintained on room air, urine output being nil for 12 hours. Abdomen was tense distended with generalized tenderness and guarding over lower abdomen. On per speculum examination, vagina and cervix appeared healthy; on per vaginal examination, uterus size could not be assessed, fullness being present in all three fornices except anteriorly, a tense cystic mass measuring approximately 14 cm × 16 cm, tender, freely mobile felt in the left fornix, and a tense cystic mass measuring 10 cm × 10 cm, tender, freely mobile felt in right fornix. On admission, urine pregnancy test was negative. On transabdominal ultrasound imaging as seen in Figure 1, there was moderate ascites with right ovary measuring 12 cm × 10 cm × 8 cm, left ovary measuring 15 cm × 12 cm × 10 cm, with both ovaries having multiple variable-sized well-defined cysts.


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Fig. 1: Ultrasonogram (USG) showing bulky ovary with large follicles
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Table 1: Investigation monitoring

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Pre-operative</th>
<th>Post-operative day 2</th>
<th>Post-operative day 10</th>
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<tbody>
<tr>
<td>Hemoglobin (gm/dL)</td>
<td>8.8</td>
<td>7</td>
<td>6.5</td>
</tr>
<tr>
<td>TLC (mm&lt;sup&gt;3&lt;/sup&gt;)</td>
<td>44,300</td>
<td>32,700</td>
<td>62,100</td>
</tr>
<tr>
<td>Platelets (mm&lt;sup&gt;3&lt;/sup&gt;)</td>
<td>64,000</td>
<td>122,000</td>
<td>96,000</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>56</td>
<td>62</td>
<td>68</td>
</tr>
<tr>
<td>Creat (mg/dL)</td>
<td>5.8</td>
<td>5.5</td>
<td>7</td>
</tr>
<tr>
<td>Total Proteins (gm/dL)</td>
<td>3.6</td>
<td>4.2</td>
<td>4</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>30</td>
<td>76</td>
<td>130</td>
</tr>
<tr>
<td>D-dimer (ng/mL)</td>
<td>&gt;3,000</td>
<td>&gt;3,000</td>
<td>&gt;3,000</td>
</tr>
<tr>
<td>Fibrinogen (mg/dL)</td>
<td>230</td>
<td>170</td>
<td>76</td>
</tr>
</tbody>
</table>

Fig. 2: Enlarged ovaries with multiple cysts

with few of them showing echogenic content within. The patient was admitted in intensive care unit (ICU) and was monitored closely as shown in Table 1, multiple cycles of hemodialysis for acute renal failure were given, prophylactic anticoagulation therapy with low molecular weight heparin was started, 0.5-mg cabergoline<sup>5</sup> was added and fluid therapy was continued. On day 2 of medical therapy, drop of hemoglobin to 4.8 gm/dL and an increase in abdominal girth by 10 cm associated with tenderness was noticed. An ultrasound was advised which revealed ascites with echoes and diagnostic tapping confirmed hemoperitoneum. The patient was immediately shifted for an emergency exploratory laparotomy. Intraoperatively 800 cc of hemoperitoneum was drained, bilateral large multicystic ovaries as shown in Figure 2 were seen of which the right ovary measured 12 cm × 10 cm × 10 cm and the left ovary measured 15 cm × 12 cm × 10 cm with partial torsion and a capsular rupture measuring 1.5 cm × 2 cm. After performing left salpingo–oophorectomy, right ovarian cyst aspiration was done. An abdominal drain was inserted and the patient was shifted to post-surgical ICU for monitoring. Immediately post-operatively the patient was kept on mechanical ventilation, transfused blood, and started on broad spectrum antibiotics such as piperacillin tazobactam combination. On day 2 post-operatively, she was extubated and maintained saturation on room air. From day 2 to day 8 post-operatively, the patient was closely monitored and given alternate day hemodialysis as advised by the nephrologist. The drain output kept reducing and was removed on post-operative day 6. On day 9 the patient had dyspnea with a drop in saturation, she was reintubated, chest X-ray was advised which was suggestive of bilateral pleural effusion. By day 11, the patient suffered from multiple organ failure and succumbed to death.

Discussion

Egg donation is a part of ART wherein the donor receives multiple hormonal drugs to stimulate the ovaries to produce multiple mature oocytes in one menstrual cycle.

The process consists of two phases, namely, the first being ovarian hyperstimulation and the second phase of egg retrieval.

The first phase consists of creating an artificial menopause by giving gonadotropin releasing hormone agonist analogs which suppresses the release of luteinizing hormone (LH). This is then followed by a daily administration of follicle stimulating hormone (FSH) which encourages the development of multiple egg follicles. Once eggs have matured, the ovulation is triggered by a single injection of human chorionic gonadotropin (hCG). Hence, a certain degree of hyperstimulation is desirable but it should be distinguished from an exaggerated response which can be potentially life-threatening.

Ovarian hyperstimulation syndrome can be early or late, early occurs within 9 days of exogenous (hCG) administration, while late occurs after 10 days and is related to endogenous hCG production. The syndrome is characterized by ovarian enlargement, pleural and peritoneal effusion, oliguria, liver damage, and thromboembolism.

The risk factors for OHSS include younger age, higher levels of LH in cases of polycystic ovarian syndrome, estradiol levels above 3,000 pg/mL, 20 or more small follicles, trigger with hCG, FSH/LH causes higher incidence of OHSS than clomiphene and GnRH.<sup>6</sup> The prevention of OHSS is possible by “coasting” which is a strategy to postpone the administration of hCG in women with high levels of estradiol (>3,000 pg/mL) until this falls to safe levels.<sup>7</sup> Giving albumin 5% infusion during and after oocyte retrieval and dopamine agonist vascular endothelial growth factor (VEGF) agonist cabergoline 0.5-mg daily for 8 days starting on day 1 of hCG can prevent OHSS.

Management of OHSS is mainly supportive and consists of correction of hypovolemia, thromboembolism prophylaxis with anticoagulants like heparin, and dopamine agonists to improve renal blood flow and prevent renal failure.

Patients are closely monitored with complete blood counts, hemoglobin, hematocrit, fluid input output measurements, blood urea levels, electrolyte estimation, liver and kidney function tests, weight gain, and ultrasound monitoring of ovarian cyst and ascites.
Surgical management is reserved for cases of ovarian cyst rupture, hemoperitoneum, and ovarian torsion.

Hence, the patients with OHSS should be identified early and treated aggressively, if not it can result in serious health complications and even death.

References