Severe Ovarian Hyperstimulation Syndrome Coexisting with a Bilateral Ectopic Pregnancy

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Management of severe ovarian hyperstimulation syndrome (OHSS) includes hospitalization for fluid and electrolyte management. Abdominal paracentesis is also used as minimally invasive form of management in selected cases of severe OHSS following ovulation induction. However, if pregnancy ensues, the syndrome persists for a longer period, and the clinical manifestations of severe OHSS could mask the picture of a bleeding gestational sac. It could be easily overlooked unless the possibility of an ectopic pregnancy is kept in mind in cases of severe OHSS exacerbated by early pregnancy with or without a previous ectopic pregnancy history. We report a case of severe OHSS with simultaneous bilateral tubal pregnancy following intrauterine insemination (IUI). A 31-year-old woman with polycystic ovarian disease developed severe OHSS during the therapeutic course of IUI. An emergent exploratory laparotomy was performed 14 days after admission, and the operative findings showed persistent profuse bleeding from the bilateral fimbrial ends with marked enlargement of the ampullary portions. A linear salpingotomy was performed by a longitudinal incision along the area of maximal distension of the dilated fallopian tubes to preserve her fertility. We recommend that in cases of severe OHSS exacerbated by early pregnancy, serial serum β-hCG and transvaginal ultrasound follow-up may be necessary due to the potential association of severe OHSS in pregnancy with an ectopic pregnancy. *(Chang Gung Med J 2004;27:143-7)*

Key words: ovarian hyperstimulation syndrome, ectopic pregnancy, intrauterine insemination.

Ovarian hyperstimulation syndrome (OHSS) is a potentially life-threatening condition associated with ovulation induction. In its severe forms, the syndrome is characterized by ovarian enlargement, ascites, hemoconcentration, hypercoagulability, pleural effusion, oliguria, and liver function abnormalities. The patient may present with severe abdominal discomfort, dyspnea, and decreased urine output.

Abdominal paracentesis and intensive IV fluid therapy are generally used to improve the patient's general condition by reducing dyspnea and improving urine output. However, the clinical presentation of severe OHSS can mask a diagnosis of a bleeding gestational sac and make it very difficult to diagnose the coexistence of OHSS with an ectopic pregnancy. We report a case of severe OHSS with simultaneous bilateral tubal pregnancy following intrauterine insemination (IUI) and review those cases reported in the literature.

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CASE REPORT

A 31-year-old woman with a 4-year history of primary infertility underwent an IUI cycle. Complete infertility evaluation had previously yielded a diagnosis of polycystic ovarian disease. During the first half of that year, she had developed oligomenorrhea (40 to 45 days per cycle) and had received clomiphene citrate (Clomid; Merrel-Dow, Neuilly-sur-Seine France) for 4 cycles, but the ovarian response was inadequate.

She had received 100 mg of clomiphene citrate for 5 consecutive days beginning on days 3 to 5 and 2 ampules/day of human menopausal gonadotropin (hMG, Pergonal; I.F. Serono, Rome, Italy) on days 5 to 10. A baseline transvaginal ultrasound scan was performed at the start of the treatment cycle to exclude any residual cyst. Repeated ultrasound scans were done between cycle days 10 and 12 to confirm follicular development. The serum estradiol (E2) concentration on day 12 was 2512 pg/ml. An ultrasound scan at that time revealed 10 large follicles in the left ovary (mean diameter, 18±2.1 mm) and 7 large follicles in the right ovary (mean diameter, 19±2.2 mm). Human chorionic gonadotropin (hCG) at 10,000 IU was given when the mean diameter of the leading follicle reached 18 mm. Swim-up and Percoll gradients were indiscriminately employed for insemination using her husband's sperm. Intrauterine insemination was performed 36 h after IM hCG administration on day 14. The luteal phase was supported with 100 mg/day micronized progesterone (Utrogestan, Lab Besins-Iscovesco, Paris, France). She was also informed of the possible risk of developing OHSS and was instructed to maintain regular follow-ups at our outpatient units.

Nine days after insemination, the patient was awakened from sleep by a sharp, intermittent bilateral lower quadrant abdominal pain. The patient returned to our center with a greatly distended abdomen, and associated symptoms of nausea, vomiting, dyspnea, constipation, oliguria, and weight gain.

On admission, her vital signs were stable: a pulse rate of 95/min, temperature of 36.5˚C, and blood pressure of 120/85 mmHg. Hematocrit, electrolytes, plasma proteins, a complete blood count, and the creatinine clearance rate were also recorded daily during hospitalization. Laboratory evaluation was significant with a hematocrit of 47%, a white blood count of 17,500/mm, serum sodium of 131 mEq/L, serum albumin of 2 g/dL, serum E2 of > 3500 pg/mL, and serum progesterone of > 40 ng/mL. Renal and liver function studies were normal.

Abdominal sonography revealed bilateral greatly enlarged ovaries (mean diameter of the right ovary of 20.4 cm and of the left ovary of 22.5 cm) with a massive amount of intraperitoneal fluid. A chest X-ray revealed bilateral pleural effusions. The patient was treated with bed rest and intravenous fluid replacement with a normal saline solution and 25% human albumin solution, which is routine policy in the management of severe OHSS in our program.

By the 4th day of hospitalization, the dyspnea had further deteriorated, and we decided to perform abdominal paracentesis. Three liters of an amber-colored fluid was drained. Temporary diuresis occurred, which resulted in marked improvement of the pulmonary distress. The serum β-hCG concentration was 85.6 mIU/ml the following day. A transvaginal sonographic examination revealed an empty uterus, but the endometrium was thickened (single layer of 12 mm); a diagnosis of severe OHSS exacerbated by early pregnancy was established. Shortly thereafter, 3 more paracentesis were performed on the 6th, 8th, and 11th days of hospitalization, at which time 2, 2.5, and 2.5 L of amber-colored ascitic fluid were removed, respectively. Two liters of the albumin solution along with 2 L of a normal saline solution was given intravenously after each paracentesis. On the 14th day of hospitalization, the patient had recurrent severe ascites, persistent low abdominal distension and tenderness, marked muscle rigidity, and shortness of breath. Subsequently, the patient's hemoglobin concentration progressively decreased from an initial level of 11.9 to 8.2 mg/dl. We decided to perform an exploratory laparotomy for early recognition of the underlying illness.

After a midline incision, an emergent exploratory laparotomy was performed, and massive blood-tinged ascites (2.5 L) and bilateral greatly enlarged ovaries (right ovary, 20×18 cm and left ovary, 22×20 cm) with elongated, swelling oviducts were found. We also took note of persistent profuse bleeding from the bilateral fimbrial ends with marked enlargement of the ampullary portions, without evidence of torsion of the hyperstimulated

ovaries. Other than that, no active bleeding site was found in the pelvis. A linear salpingotomy was performed by a longitudinal incision along the area of maximal distension on the antemesosalpinx side of the dilated fallopian tubes. An approximately 30~35-mm incision was made with the use of an insulated microdiathermy needle (Martin, Stanford, CT) with a shaft of 100 mm (with the cutting current set to 2 or 12 W). A solution of diluted vasopressin (1 ml in 20 ml of physiologic saline) was injected into the adjacent mesosalpinx and into the wall of the tube on the area of maximal distension before the incision was made. When the antimesenteric area of the tube was opened, dark brownish fluid with trophoblast-like tissue was gently taken out of the tube. Standard microsurgical techniques and liberal irrigation with physiologic saline were used during the procedure. The salpingotomy was closed by interrupted sutures of 6-0 Vicryl (Ethicon, Sommerville, NJ). The histologic examination of the 2 specimen sites confirmed the presence of villi, which was consistent with ectopic gestations.

The patient was discharged 5 days after the operation. She recovered uneventfully, and serial serum β-hCG titers dropped until they reached an undetectable level 3 weeks after surgery.

DISCUSSION

Ovarian stimulation in combination with intrauterine insemination is an accepted treatment for different causes of infertility.[1] Induction of ovulation with clomiphene citrate is widely used as the first choice of treatment, and failure to conceive after 6 ovulatory cycles or failure to ovulate after 3 cycles on maximal doses is considered clomiphene failure.[2] The choice of treatment for clomiphene-resistant anovulation associated with polycystic ovary syndrome (PCOS) is presently arbitrary and cannot be guided by the basal or endocrinological features of this syndrome.[3] There is also a trend toward increased pregnancy rates when human menopausal gonadotropins, rather than clomiphene citrate, are employed.[4]

OHSS manifests as ovarian enlargement with multiple follicular and lutein cysts. If pregnancy ensues, the syndrome persists for a longer period. This is probably because of continued exposure of the ovaries to endogenous β-hCG. Severe forms of ovarian hyperstimulation are generally treated by hospitalization, correction of the electrolyte imbalance, volume replacement with intravenous fluids (low molecular weight dextran and albumin), bed rest, and careful monitoring of urinary output, which are hallmarks of the medical management.[5] Abdominal paracentesis is a form of surgical management used in selected cases of severe ovarian hyperstimulation following ovulation induction.[6]

To our knowledge, a healthy mobile oviduct is essential for ovum pick-up from the uncovered surface of the ovary, and any periovarian or peritubal adhesion may interfere with this mechanism. It is commonly accepted that tubal infection is the major etiologic factor causing intraluminal tubal adhesion creating blind passages in which the fertilized ovum can be trapped. Controlled ovarian hyperstimulation (COH) results in a considerable increase in ovarian size and changes in the tubo-ovarian relationship. In addition, McBain et al.[7] and Gemzell et al.[8] have reported a higher rate of ectopic pregnancy in patients treated for induction of ovulation with human gonadotropins. They postulated that the high levels of estrogen caused by induction of ovulation induce abnormal tubal embryo transport; and the more eggs ovulated, the more likely they are to remain behind in the tube.

It is difficult to diagnose an ectopic pregnancy coexisting with severe OHSS at an early time. Diagnosis of a tubal ectopic pregnancy by transvaginal ultrasound at this stage is not always possible. The absence of an intrauterine sac does not exclude the possibility of an intrauterine pregnancy, as a normal sac may not be detected at this stage of amenorrhea and with the low levels of β-hCG. Abnormal pregnancies are associated with an increase in β-hCG at a rate of < 66% in 48 hours, but 15% of normal pregnancies may show an abnormal β-hCG rise. In addition, the presence of large ovaries filling up the pelvis makes ultrasound (US) scanning of other structures difficult. It is our opinion that in cases of severe OHSS exacerbated by an early pregnancy, serial serum β-hCG and transvaginal US follow-up may be necessary for the early diagnosis of an ectopic pregnancy complicated with severe OHSS.

Cases of adnexal torsion have been reported in association with OHSS,[5,9-11] but there is no information on the clinical picture or the incidence of twisted adnexa in pregnant patients with OHSS. OHSS in

pregnancy is a risk factor for developing torsion, which should increase the index of suspicion, and thereby facilitate early diagnosis and treatment.[12] The accuracy of a preoperative diagnosis of adnexal torsion during pregnancy is only 70%.[9] This remains a diagnostic challenge for gynecologists.

A review of the literature revealed that Aboulghar et al.[13] reported a case of severe OHSS complicated by an ectopic pregnancy. In that case, the patient had a previous history of having undergone a laparoscopy followed by a laparotomy for a right tubal ectopic pregnancy, and the surgical procedure performed was to expel the gestational sac from the fimbrial end. Five years later, during IUI treatment, she developed severe OHSS complicated with recurrence of a right tubal ectopic pregnancy. Finally, she underwent a right salpingectomy for her illness. However, in our case, the operative findings showed simultaneous bilateral tubal ectopic pregnancies with bleeding gestational sacs. We performed a bilateral tubal salpingotomy in order to preserve the patient's fertility. It is also well accepted that salpingotomies have gradually replaced salpingectomies as the surgical procedure of choice for an ectopic pregnancy in patients who are hemodynamically stable. According to her past history, the patient had not previously undergone any operative procedure. There was no evidence of pelvic inflammation during the pelvic examination. Consequently, tubal pathology may not have been the sole factor responsible for the tubal ectopic pregnancy in our case. We emphasize the importance of bearing in mind the possibility of an ectopic pregnancy in cases of severe OHSS exacerbated by an early pregnancy with or without a previous ectopic pregnancy history.

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卵巢過度刺激症候群合併子宮外孕

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對於卵巢過度刺激的病患除了需要入院控制電解質及輸液的給予外，尚必須以超音波引導抽取腹腔內腹水做爲治療。一旦病患妊娠試驗呈陽性反應合併卵巢過度刺激症侯群時，常常因爲卵巢過度刺激的臨床表徵，讓我們忽略了子宮外孕的可能性。本病例報告中，一位31歲婦女因多囊性卵巢，在門診接受人工授精（IUI）療程中，併發卵巢過度刺激症侯群，住院期間除了給予輸液治療及抽取腹腔內腹水等保守性治療外，於入院後第14天因持續性下腹痛並抽出血樣性腹水，予以剖腹探查。術中呈現雙側輸卵管壺腹部膨大併雙側輸卵管繖部持續性鮮紅色血液滲出，經過雙側輸卵管線狀切開造口術後，取出內含子宮外孕妊娠組織並縫合所切開的造口，以保存病患雙側輸卵管。卵巢過度刺激症侯群合併子宮外孕的情形，相當不容易診斷，除了臨床表徵之外，持續的血中絨毛膜激素濃度及經陰道超音波的追蹤對於早期診斷應該有所助益。(長庚醫誌 2004;27:143-7)

關鍵字：卵巢過度刺激症侯群，子宮外孕，人工授精。

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