Pulmonary edema complicating ovarian hyperstimulation syndrome: low-pressure edema, high-pressure edema, or mixed edema?

Ahmed S. BaHammam

Ovarian hyperstimulation syndrome (OHSS), a serious iatrogenic complication of ovulation induction treatment, is associated with substantial morbidity and occasional mortality.[1] OHSS is characterized by increased capillary leak with massive transudation of protein-rich fluid from the vascular space into the peritoneal, pericardial, and pleural cavities and alveoli.[1] Serious respiratory manifestations complicate this disorder, including pulmonary edema, pulmonary embolism, and massive pleural effusion, which may necessitate admission to the intensive care unit (ICU). Pulmonary edema complicating OHSS has been reported as low-pressure edema, and OHSS patients with pulmonary edema requiring ICU admission have been diagnosed with acute respiratory distress syndrome (ARDS).[2] We report a patient with severe OHSS complicated by acute respiratory failure, bilateral alveolar infiltrate, and a high pulmonary capillary wedge pressure (PCWP), with good response to diuresis and fluid restriction and good correlation between PCWP and PaO_2/FiO_2 (arterial oxygen pressure/fraction of inspired oxygen).

Case

A 29-year-old woman with secondary infertility and mild bronchial asthma, and no other known medical problems, presented to the emergency room (ER) in our hospital with progressive lower abdominal pain radiating to the back, associated with abdominal distension and nausea. She also complained of mild dyspnea. The patient was being treated for infertility in a private clinic, where she had been given 14 injections of both Metrodin (Serono, Switzerland) and Pergonal (Serono, Switzerland) on days 3 to 9 of her cycle. On day 12, human chorionic gonadotropin was given. The doses were not documented. She presented to the ER with the above symptoms on the nineteenth day of her cycle.

Examination revealed a young lady in pain and distress. Vital signs were stable. Her abdomen was distended with generalized tenderness and ascites. Chest and cardiac examinations were unremarkable. A basic blood work-up showed an elevated white blood cell (WBC) count of 11 000 with 90% neutrophils, hemoglobin 149 g/L, and hematocrit 45%. Arterial blood gas (ABG), renal, hepatic, and coagulation parameters were normal. A chest radiograph showed basal atelectasis. A pregnancy test was negative. Pelvic ultrasound showed grossly enlarged ovaries (left ovary: 19 centimeters, right ovary: 17 centimeters) with a 6-centimeter cyst in the right ovary and gross ascites.

The patient was admitted to the ward for observation and hydration. While in the ward, she maintained a urine output of 1.0 to 2.5 L/day. Her condition continued to deteriorate in terms of progressive respiratory distress and increasing abdominal pain and distension. On the

From the King Saud University, Respiratory Unit, Department of Medicine, College of Medicine, Riyadh, Saudi Arabia

Correspondence:
Dr. Ahmed Bahammam, FRCP, FCCP
Associate Professor
King Saud University
Respiratory and Critical Care Unit, College of Medicine, Department of Medicine 38
P.O. Box 2925
Riyadh, 11461
Saudi Arabia
Tel: 966-1-467-1521
Fax: 966-1-467-2558
ashammam2@yahoo.com

Accepted for publication:
March 2004

Ann Saudi Med 2005;25(4):335-338

fourth admission day, the patient started to have hemoptysis and hypoxemia [ABG on room air was pH 7.44, PaO_2 64 mm Hg (8.4 kPa), $PaCO_2$ 32 mm Hg (4.3 kPa), bicarbonate 21.8 mmol/L, and O_2 saturation 94%]. A ventilation-perfusion lung scan and duplex ultrasound of the legs were normal.

On the fifth admission day, the patient was transferred to the intensive care unit (ICU) due to severe respiratory failure and refractory hypoxemia. On arrival at the ICU, she was in great distress, was afebrile, could not lie flat, and had a jugular venous pressure (JVP) of 9 centimeter H_2O with mild lower-limb edema. Her blood pressure was 130/90 mm Hg, heart rate 130/min, and respiratory rate 50/min. Chest examination revealed diminished breath sounds with bilateral expiratory wheeze and inspiratory crackles. The abdomen was distended and tender all over. Her fluid balance over the previous few days was estimated to be 6-7 L on the positive side (Figure 1). Chest radiograph showed extensive bilateral alveolar infiltrates (Figure 2a). Her WBC count was 18 000, hemoglobin level 120 g/L, hematocrit 27%, and serum sodium 145 mmol/L; renal, hepatic, and coagulation parameters were normal. Inhaled steroids and bronchodilators were administered.

Within a short period of ICU admission, the patient's condition necessitated mechanical ventilation with 100% O_2 (FiO_2 of 1) and a positive end expiratory pressure (PEEP) of 5 cm H_2O. Peak airway pressure was 42 cm H_2O and plateau pressure was 38 cm H_2O. However, due to refractory hypoxemia, the patient was given muscle relaxants and adequate sedation. PEEP was increased in successive steps to 10 cm H_2O and the inspiratory:expiratory ratio was adjusted to 1:1.2. A pulmonary artery catheter (Swan-Ganz catheter) (before starting ionotropes) showed a pulmonary capillary wedge pressure (PCWP) of 23 mm Hg, central venous pressure of 17 mm Hg, cardiac index of 5.6 L/min/m^2, and systemic vascular resistance of 660 DS/cm.[5] She developed hypotension, initially necessitating administration of dopamine and then noradrenaline (0.5-2 microgram/min) with a small dose of dopamine (2.5 microgram/kg/minute). The patient remained afebrile during her stay in the ICU. Fluid restriction and diuretics were instituted. Figure 1 shows the relationship among PCWP, fluid balance, and PaO_2/FiO_2. A negative fluid balance resulted in a reduction in PCWP, which in turn produced improvement in the PaO_2/FiO_2. The patient was extubated on the sixth day after ICU admission. The chest radiograph on discharge from the ICU is shown in Figure 1b. She was discharged home 5 days later. Clinical evaluation and echocardiogram 3 months later were normal.

Discussion

ARDS is a rare complication of OHSS.[2-5] Although the exact pathophysiology of ARDS in OHSS is not clear, it is thought that increased capillary permeability, triggered by the release of vasoactive substances like vascular endothelial growth factor (VEGF) secreted by the ovaries, plays a major role,[6,7] based on the findings in an autopsy case of OHSS, where the authors proposed increased progesterone as a potential cause of increased capillary leak and pulmonary edema. However, ARDS complicating OHSS has been reported to occur after massive hydration and to resolve rapidly after fluid restriction and administration of loop diuretics.[4] In ARDS patients, the above interventions usually help but do not result in quick recovery. This raises the question: is pulmonary edema in OHSS low-pressure edema, high-pressure edema, or mixed edema?

Zosmer et al.[2] documented low PCWP in a patient with OHSS and demonstrated marginal improvement in respiratory failure after reducing PCWP. On the other hand, others have diagnosed patients with OHSS complicated by respiratory failure and bilateral alveolar infiltrate as ARDS patients without measuring PCWP.[3,4] Recently, in an autopsy case of OHSS, Semba et al[7] reported massive pulmonary edema without diffuse alveolar damage, hyaline membrane formation, or interstitial inflammatory infiltrate. Here, we report a classical case of acute respiratory failure and diffuse alveolar infiltrate complicating OHSS after massive hydration, with rapid improvement after fluid restriction and diuresis. However, we found high PCWP on admission to the ICU and significant improvement in respiratory failure and oxygenation associated with the reduction in PCWP. In addition to capillary leakage into the alveoli, we consider that this OHSS patient developed high-pressure pulmonary edema. Her rapid response to fluid restriction and diuretics favors fluid overload and high-pressure edema as a possible mechanism for the respiratory failure and for the diffuse alveolar infiltrate seen on the chest radiograph. It has been demonstrated that patients with OHSS have hyperdynamic circulation with increased cardiac output and decreased systemic vascular resistance.[8] In addition, plasma concentration of atrial natriuretic peptide has been shown to increase in patients with OHSS.[8] These observations support the argument that patients with OHSS may have circulatory dysfunction.

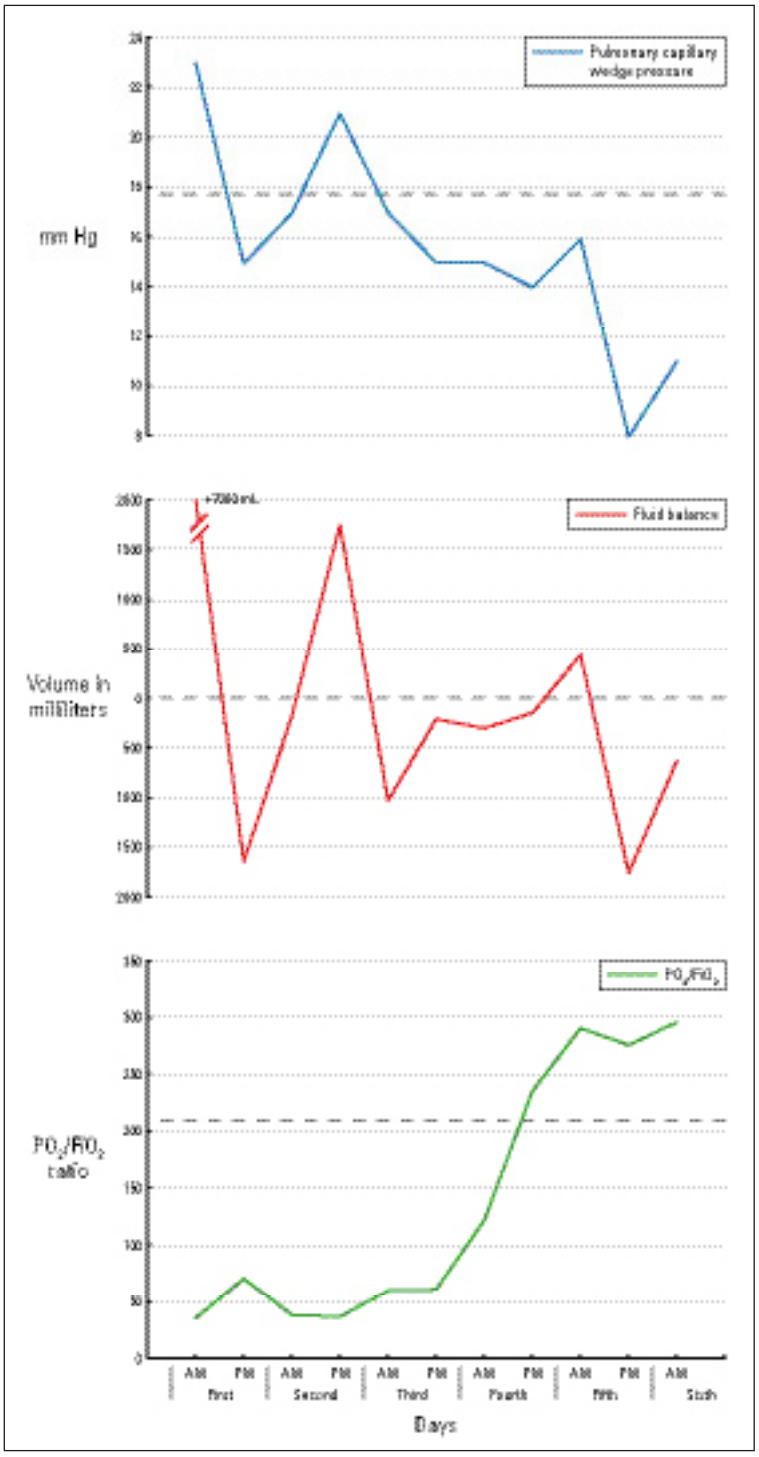

Figure 1. The relationship among PCWP, fluid balance, and PaO_2/FiO_2. The x-axis represents the days of ICU admission. Measurements were taken twice daily: AM (05:00) and PM (17:00). Fluid balance represents the balance over 12 hours.

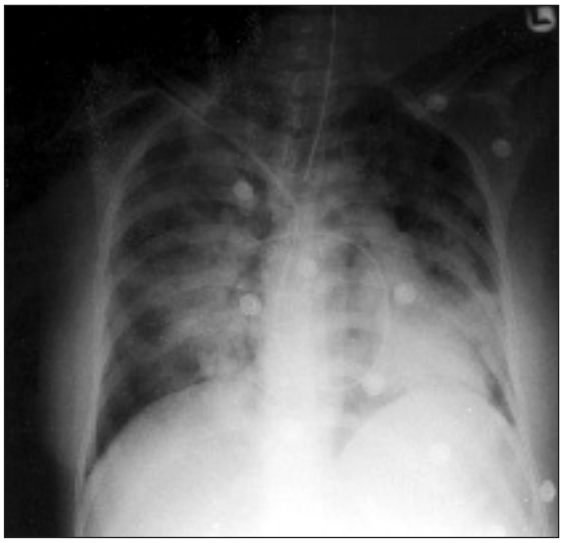

Figure 2a. Chest radiograph on admission to the ICU, showing extensive bilateral alveolar infiltrates.

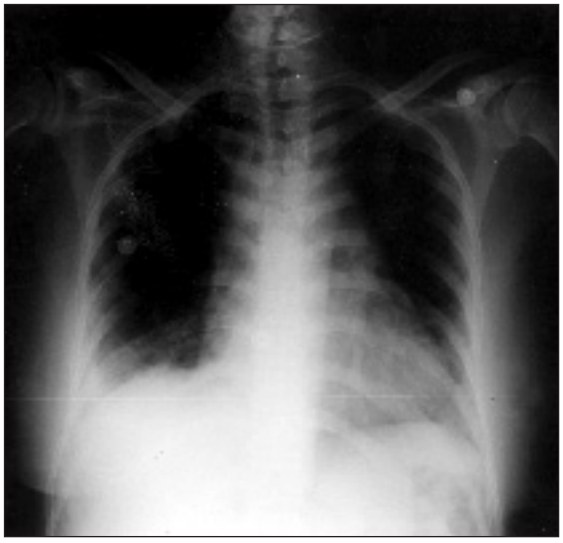

Figure 2b. Chest radiograph on discharge from the ICU.

In summary, pulmonary edema is a rare but serious complication of OHSS. Increased capillary permeability has been proposed as the likely mechanism, resulting in low-pressure pulmonary edema. However, some patients with OHSS may be prone to developing high-pressure edema, which exacerbates the already existing edema from capillary leakage, forming a mixed type of pulmonary edema. In this group of patients, vigilant attention to fluid management, frequent titration of intravenous fluid, and diuresis to maintain euvolemia may avert critical-care respiratory sequelae. In OHSS patients who require ICU admission due to respiratory failure, PCWP monitoring can help greatly in guiding fluid management.

References

1. Whelan GJ, Vlahos NF. The ovarian hyperstimulation syndrome. *Fert Sterl*. 2000;73:883-896.
2. Zosmer A, Katz Z, Lancet M, Konichezky S, Schwatz-Shoham Z. Adult respiratory distress syndrome complicating ovarian hyperstimulation syndrome. *Fertil Steril*. 1987;47:534-526.
3. Myrianthefs P, Ladakis C, Lappas V, Pactitis S, Carouzou A, Fildisis G, Baltopoulos G. Ovarian hyperstimulation syndrome (OHSS): diagnosis and management. *Intensive Care Med*. 2000;26:631-634.
4. Abramov Y, Elchalal U, Schenker J. Pulmonary manifestations of severe ovarian hyperstimulation syndrome: a multicenter study. *Fertil Steril*. 1999;71:645-651.
5. Shigematsu T, Kubota E, Aman M. Adult respiratory distress syndrome as a manifestation of ovarian hyperstimulation syndrome. International *J Gyne Obstet*. 2000;69:169-170.
6. Elchalal U, Schenker JG. The pathophysiology of ovarian hyperstimulation syndrome—views and ideas. *Hum Reprod*. 1997;12:1129-1137.
7. Semba S, Moriya T, Youssef EM, Sasano H. An autopsy case of ovarian hyperstimulation syndrome with massive pulmonary edema and pleural eefusion. *Pathology Internatonal*. 2000;50:549-552.
8. Balasch J, Arroyo V, Fábregues F, Saló J, Jiménez W, Paré JC, Vanrell JA. Neurohormonal and hemodynamic changes in severe cases of the ovarian hyperstimulation syndrome. *Ann Intern Med*. 1994;121:27-33.