Pleurisy in ovarian hyperstimulation syndrome: A case report

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ABSTRACT

Exogenous gonadotrophins are frequently used now for the induction of ovulation. Ovarian hyperstimulation syndrome (OHSS) is well-recognized complication of this treatment and can present in a number of ways including pleurisy and acute respiratory failure. We report a 23 year old Saudi lady with OHSS who developed acute hypoxemia and large bilateral exudative pleural effusions and discuss the thoracic manifestations of OHSS.

Keywords: Ovarian hyperstimulation syndrome, gona-dotrophins, respiratory complications, pleural effusion.


Exogenous gonadotrophins are now used frequently for women with infertility. Physicians need to be aware of the possible complications that may arise occasionally. Ovarian hyperstimulation syndrome (OHSS) is a serious, potentially life-threatening complication that may lead to fluid depletion, shock, renal failure and thromboembolism. Thoracic involvement has been reported infrequently in OHSS. Herein, we report a patient who developed acute respiratory distress and exudative pleural effusions after receiving treatment for induction of ovulation.

Case Report. A 23 year old Saudi lady was seeking medical assistance for infertility at King Khalid University Hospital since 1993. She underwent full evaluation, including a diagnostic laparoscopy, and was found to have polycystic ovaries. An initial attempt to induce ovulation using six cycles of clomiphene citrate (clomid) starting at 50mg then 100 mg was unsuccessful. Induction of ovulation by gonadotrophins was then tried. She received human menopausal gonadotrophin (HMG, pergonal) intramuscularly starting at 150 units for the first two days. Over the following week she was given 14 ampules of pure follicular stimulating hormone (FSH, metrodin) and 4 ampules of pergonal. She was monitored by serial ultrasonic examinations of the ovaries for growing follicles and hormonal assay of serum estradiol level. The ultrasound showed 10 to 12 growing follicles in both ovaries, up to 11 mm in diameter at day 12 of menstrual cycle, while estadiol level was 176 pmol/L. By day 16, the size of the leading follicles increased to 25 x 18 mm, and estadiol level rose to 3628 pmol/L. To trigger ovulation human chorionic gonadotrophin (HCG, pregnyl) 5000 IU was administered the following day. Later in the same day, the patient complained of abdominal pain. Ultrasound showed both ovaries containing follicles of around 5 cm. She was suspected of having a mild hyperstimulation of ovaries. At that stage her weight was 90 kg and

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abdominal girth was 100.5 cm. Urea and electrolytes were within normal limits. Forty-eight hours later the patient was still complaining of abdominal pain. Her chest was clinically clear. She was receiving intravenous fluids to maintain her fluid status. Serum electrolytes, urea and creatinine continued to be normal. Serum protein was 59 g/l. Six days after HCG injection the patient developed dyspnea. Examination of her chest showed dull percussion note and diminished breath sounds at the right base. Cardiovascular examination was normal. Abdominal examination revealed mild ascites. Her weight increased to 95 kg and abdominal girth to 107.5 cm. Both ovaries were containing cysts about 10 and 13 cm each. Arterial blood gas (ABG) showed the following: pH 7.37, Pa CO₂ 31.5 mm, Hg Pa O₂ 89.7 mmHg, and HCO₃ 18.7 mmol/L. Chest radiograph showed homogeneous shadow in the right base obliterating the right costophrenic angle. Over the next few days her dyspnea and chest pain became worse and her PaO₂ dropped to 64.5 mm Hg. Chest radiograph revealed progressive increase in the shadows with involvement of the left side as well (Fig.1). A decubitus film confirmed the presence of free pleural fluid. Full blood count showed a normal leukocyte count and differential, and a hemoglobin of 131 g/L (which had risen from a base line value of 119 g/L) and normal platelets. Serum electrolytes, urea and creatinine, liver function tests and coagulation profile were within normal range. A Duplex ultrasound of lower extremities revealed no evidence of deep vein thrombosis. A perfusion ventilation scan showed matched defects indicating a low probability scan for pulmonary embolism. Estradiol level increased further to reach a peak of 10161 pmol/L. A diagnostic pleural tap showed the following: protein 42 g/L, LDH 114 lũ/L, glucose 5 mmol/L, leukocyte count 1200/mm³ (30% polymorphs, 70% lymphocytes).

During her ICU stay she was managed with supplemental oxygen, intravenous fluids and prophylactic sub-cutaneous heparin. Subsequent assays of estradiol showed a drop to 4910 pmol/L and ultrasonographically the cysts started shrinking. She had complete recovery within six days from the onset of the symptoms. This attempt to induce ovulation did not result in pregnancy.

**Discussion.** Although OHSS is an infrequent complication of ovulation induction therapy, more cases are likely to be seen because of the increasing use of this mode of therapy both in government and private health sectors. Incidence of this syndrome has been estimated at 4% with about 0.25 to 0.9% being severe. The basic underlying pathophysiology is enlargement of the ovaries with a vascular leak, the cause of which is poorly understood. Defects in renin-angiotensin system, prostaglandins and other endothelial factors have been implicated. In severe cases this leads to fluid depletion, third-space fluid shifts, hemoconcentration, renal insufficiency, electrolyte imbalance, massive ascites and pleural effusion and thromboembolism.

Risk factors for development of this condition include young age, polycystic ovaries, sensitive ovarian response to gonadotrophins (indicated by the level of estradiol), high number of follicles and administration of HCG. All these factors were present in our patient. Thoracic involvement in OHSS is relatively infrequent, with pleural effusion being the most frequently reported manifestation. Since only a small number of case reports are available, the characteristics of the pleural fluid are not well elucidated. In most of these reports the fluid was found to be exudate. In our patient the effusion was bilateral, exudative, with a normal LDH and glucose and leukocytes were predominantly lymphocytic. Other respiratory manifestations also include atelectasis, V/Q mismatch and ARDS. Hypoxemia may occur due to any one of these factors, in addition to restriction by ascites if present in significant quantities. In our patient the most likely cause for hypoxemia is the significant pleural collection with atelectasis, although a degree of interstitial pulmonary edema cannot be excluded. Although OHSS may be associated with thromboembolism, the
finding of a matched defect on the ventilation perfusion scan makes pulmonary embolism an unlikely diagnosis.

Respiratory failure associated with OHSS is managed in the usual way, by admission to the intensive care unit and careful monitoring and correction of oxygen, fluid and protein status. Abdominal paracentesis and thoracostomy tube drainage may be needed to relieve the associated respiratory distress, but since OHSS undergoes resolution in several day such measures may not be always necessary. This was the case for our patient who, despite the severity of her illness, recovered completely within 6 days with supportive treatment alone. Novel, approaches have been reported in the exceptionally very severe cases, including ascetic fluid recirculation.

This syndrome should be preventable, by considering the risk factors stated above, daily monitoring of estradiol level, frequent ultrasonography and withholding HCG in women who develop high level of estadiol and a high number of follicles. Awareness of physicians of the various manifestations of OHSS and the optimal care should also lead to a better outcome.

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References