

Case Report

Unilateral pleural effusion as the sole presentation of ovarian hyperstimulation syndrome (OHSS)

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Case presentation

A 44-year-old G4P2+1 presented to the emergency department on the 10th day following embryo transfer (with two fresh, day 5, blastocysts transferred in a hospital abroad) with the complaints of difficulty breathing, chest discomfort and cough for one day. These symptoms increased on lying on her side and were not related to exertion. She also mentioned having had abdominal discomfort over the preceding few days. On taking a past history, the patient revealed that all her prior pregnancies were the result of IVF treatment and she suffered OHSS with each. Her first pregnancy was a triplet gestation through IVF and complicated by OHSS; followed by her second pregnancy which was an IVF twin gestation also complicated by OHSS with ascites requiring paracentesis. With her third IVF treatment she conceived, had OHSS and miscarried spontaneously. However, these IVF treatments and pregnancies were all managed abroad and no medical records were available.

Examination findings included reduced breath sounds in the basal area of the right lung. As the patient's BMI was high at 38, it was difficult to clinically comment on ascites. Baseline bloods as well as an ultrasound were arranged. The bloods test results, including a complete blood count and renal and electrolyte, were normal with the serum albumin decreased at 29 g/dl and a beta HCG value of 95 mIU/ml. The ultrasound revealed enlarged ovaries consistent with ovarian hyperstimulation and no ascites, however a right sided pleural effusion was noted. With the discovery of the pleural effusion, an Internal Medicine review was sought. A chest X ray was performed which then confirmed a right sided pleural effusion. No other underlying potential cause could be identified and it was concluded that the pleural effusion was due to the ovarian hyperstimulation syndrome.

The patient was initially managed conservatively but subsequently, due to persisting dyspnea, a chest drain was

More Information

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used to drain the effusion on the third day after admission. 1350 ml of fluid were drained initially followed by another 800 ml over the next 48 hours. An analysis of the pleural effusion fluid reported the fluid as containing reactive mesothelial cells with macrophages and neutrophils. It had a high protein content of 39 gm/L (serum protein was 66 gm/L) suggesting it was an exudate. A microbiological culture was negative. The patient responded well to treatment and was discharged after a five day stay at the hospital. A subsequent scan at 2 weeks revealed bulky ovaries and a small pleural effusion. A further scan at 4 weeks was found to be normal with a single intrauterine viable pregnancy. The pregnancy progressed normally and the patient was followed up as an outpatient for antenatal care. Through the course of the pregnancy, she developed gestational diabetes requiring insulin and was delivered by cesarean section at 38 weeks gestation having had two prior cesarean deliveries. She gave birth to a healthy female infant weighing 3050 grams.

Discussion

Severe ovarian hyperstimulation syndrome is a serious complication of assisted reproduction treatment, with an incidence up to 0.5-1% of cases. While usually mild to moderate in presentation, it has the potential to develop onto a life-threatening condition.

OHSS may occur after any ovarian stimulation and after administration of human chorionic gonadotrophins (HCG).



The most common presentation of OHSS is enlarged ovaries with varying degrees of ascites, with or without concomitant pleural effusion depending on the severity. However, isolated pleural effusion is a rare presentation of OHSS and is reported in less than 1% cases. This makes it an easily missed diagnosis where, in the absence of the telltale signs like ascites, chest symptoms of an isolated pleural effusion may be missed or identified late. Further, with ascites and concomitant pleural effusion, chest symptoms like dyspnea, may be falsely attributed to ascites, delaying the diagnosis of a pleural effusion with this case, the clinical presentation was with prominent chest related symptoms only, where early imaging helped detect the pleural effusion.

The manifestations of OHSS are secondary to increased vascular permeability and fluid leakage into the extra vascular space causing ascites, pleural effusion and/or pericardial effusion. This increased permeability is mediated by some substances such as vascular endothelial growth factor, interleukins 1,2 and 6 [1].

The pathogenesis of OHSS related pleural effusion in particular may be explained by movement of ascitic fluid from high intra-abdominal pressure via lymphatic channels or congenital defects in the diaphragm to the negatively pressured pleural cavity [2]. However, the presence of pleural effusion without ascites is more difficult to explain. There are a few theories that have attempted to explain this; a pathological condition of the pleural serosa as an underlying factor was suggested by Daniel, et al. [3] while Friedler, et al. [4] noted a recurrence of the same problem with repeat treatment and suggested some local anatomical changes in the diaphragm as causative. Such defects in the diaphragm have been discovered more often on the right side during surgery such as open thoracotomy and also during some post-mortum studies [5] this is a possible explanation for the observation that unilateral pleural effusion is far more common on the right side as demonstrated in the case presented above

The pleural effusion fluid itself can be classified into two types, exudate and transudate. Exudate is rich in protein and is the result of an inflammatory process while transudate tends to have low protein content and is a result of either increased hydrostatic pressure or decreased plasma oncotic pressure [6]. Exudate pleural effusion incidence is almost double that of transudate, the occurrence of both of them in different cases would also support the theory that more than one mechanism is associated with the development of pleural effusion in OHSS. Indeed, the pleural effusion in this case was of exudate type.

The management of pleural effusion will largely depend on its severity and symptomatology, in the largest case series [7] 90% of the cases required chest drainage, draining on average 4332 ± 769 mL. Only one case had left pleural effusion and five had bilateral while 24 (80%) were right side only. Our experience with the case discussed resonates with these findings.

Preventing this complication of pleural effusion is dependent on the prevention of OHSS during IVF treatment, and all IVF units and reproductive medicine specialists must have guidelines and strategies to prevent/reduce the incidence and severity of OHSS. The first step into prevention would be to identify those at risk of OHSS.

There are few factors that may predict OHSS such as the diagnosis of polycystic ovarian syndrome, young age, high AMH level, high number of antral follicles count, high number of follicles before triggering oocyte maturation, serum estradiol level on day of trigger and high oocyte yield after retrieval are all correlating with the risk of developing OHSS. Within the case discussed, there were risk factors of previous history of OHSS on three occasions but other risk factors relating to IVF details could not be ascertained as no records were available.

Developing an individual risk assessment tool such as chart or algorithm can help identify cases at higher risk of developing OHSS, [8] developed a decision-making algorithm for cancelling embryo transfer in patients with high risk for OHSS based on different parameters on different days of the treatment cycle, These included the number of oocytes retrieved, Haematocrit, white cell count, mean ovarian diameter and grade of ascites if present. That algorithm had 88.5% sensitivity and 84.2 specificity to identify cases that will develop OHSS.

Cases that are at high risk of OHSS should be advised against fresh embryo transfer and adopt a freeze all policy and arrange for frozen embryo transfer later, other methods to reduce risk of OHSS includes using lowest possible dose of Gonadotrophins and using GnRH agonist and low dose of HCG to trigger oocyte maturation and finally cycle cancellation as a final resort.

Newer approaches such as in vitro ovarian maturation [9] and mild/minimal ovarian stimulation [10] have been shown to almost eliminate the risk of OHSS albeit with reduced life birth rate and more improvement and experience in such technique is likely to improve pregnancy rates in the future.

Conclusion

This case report emphasizes the less common yet potentially serious and life threatening complications of assisted reproduction technology (ART). Unfortunately OHSS remains under reported by many IVF centers, Data from the Human fertilization and Embryo Authority (HFEA) report just under 100 cases of OHSS in the years 2014-2015, [11]. During the same period NHS database had recorded over 800 admissions to NHS hospital with OHSS and over 95% of this admissions were emergency admissions. Risk assessment of candidates along with tailored, in-depth counselling is essential so that women can understand risks and consider accepting mitigating strategies such as starting with a low



dose of gonadotrophin, accepting less egg yield and possible delays in embryo transfer or even cycle cancellation. This is particularly important with the increasing number of women going through ART. Dyer, et al. [12], on behalf of the international committee for monitoring, ART reported that between the years 2008 and 2010 almost 4.5 million women started ART treatment cycles. Creating an awareness of this potential serious complication among ART providers as well as patients is therefore of high importance.

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