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CASE REPORT: SPONTANEOUS OVARIAN HYPERSTIMULATION SYNDROME IN A SINGLETON PREGNANCY OF A PRIMIGRAVIDA WITH HYPOTHYROIDISM.

Gynaecology

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ABSTRACT

Spontaneous Ovarian Hyper Stimulation Syndrome (OHSS) is an extremely rare and intriguing entity. In an era of increasing demand for assisted reproductive techniques, drug induced OHSS has become a commonly anticipated and encountered event. Spontaneous OHSS on the other hand requires high index of suspicion, or else misdiagnosis and unnecessary surgical intervention would complicate the scenario. This is a case of spontaneous OHSS in a primigravida at 9 weeks of planned spontaneously conceived pregnancy with primary hypothyroidism.

KEYWORDS

Ovarian hyper stimulation, Spontaneous Ovarian Hyper Stimulation Syndrome , early pregnancy, hypothyroidism , beta-hCG .

Introduction

Ovarian hyperstimulation syndrome (OHSS) in this era of assisted reproduction is a well known iatrogenic complication of ovulation induction. It is the combination of increased ovarian volume (due to multiple cysts) and vascular hyper permeability, that results in the outflow of fluid from the intra vascular space, with subsequent hypovolemia and hemoconcentration.(1) About 1 to 2% of superovulation cycles are associated with OHSS, and it remains one of the most important complications related to gonadotropin use in assisted reproductive technologies. Clinicians usually suspect this condition in iatrogenic settings and prompt management ensues. In the past few decades, it has been reported that OHSS may infrequently be associated with spontaneous ovulatory cycles. This syndrome is described in multiple pregnancy, hypothyroidism and molar pregnancies (2). The symptoms of spontaneous OHSS develop later than in iatrogenic OHSS: the syndrome occurs between 3 to 5 weeks of amenorrhea in iatrogenic cycle, and between 8 and 12 weeks of amenorrhea in spontaneous OHSS cases.(3). In absence of knowledge of spontaneous occurrence of this syndrome and high index of suspicion these cases can be mismanaged with adverse outcome.

CASE REPORT

A 26 year old primi gravida with a planned spontaneously conceived pregnancy presented at 9 weeks gestation with excessive vomiting . She was a recently diagnosed case of hypothyroidism on 25 mcg levothyroxine . An initial diagnosis of hyperemesis gravidarum was made and she was managed conservatively with anti-emetics and i.v. fluids. But her Vomiting worsened despite treatment and she developed breathlessness and abdominal distension. Investigations : An ultrasound whole abdomen showed 9 weeks pregnancy with bilateral enlarged ovaries (Right ovary 243 cc and left ovary 233 cc) along withascites and bilateral pleural effusion. Quantitative serum beta hCG was disproportionately high(1,26,780 mIU/ml). Anti-TPO antibodies were negative. In view of bilateral enlarged ovaries CA-125 , AFP and LDH were done but normal values suggested a non-malignant pathology. ANA, dDNA and fibrinogen in normal range excluded immunological causes. She was enquired again in privacy and the possibility of PCOS, ovulation induction and drug intake was excluded.

Management :

In view of early pregnancy with bilateral enlarged ovaries and polyserositis in absence of other causes , a diagnosis of spontaneous OHSS was made . The patient was shifted to ICU for multidisciplinary care . Opinions of pulmonologist, physician and immunologist were sought . A high index of suspicion was maintained and patient was treated on lines of spontaneous OHSS. Patient was closely monitored with daily weight measurement, abdominal girth charting, Input/output monitoring, biochemical tests (CBC,PCV,LFT,Beta-hCG, electrolytes). Albumin infusion , diuretics , thromboprophylaxis were administered along with oral fluids guided by thirst . She gradually improved clinically : weight reduced from 50 to 46 kgs, abdominal girth reduced from 34 inches to 32 inches, PCV from 40 to 32%. Significant reduction in ascites and pleura effusion was also observed in subsequent ultrasounds. Beta hCG levels dropped from 1,26,780 mIU/ml to 89500 mIU/ml .Ovarian volume though reduced was still 190 cc on right and 156cc on left at the time of discharge after 2 weeks of hospital stay .

Follow-up and outcome :She was kept on close OPD follow up and showed complete resolution by 20 weeks of gestation. Thereafter she was followed as a normal pregnancy and she carried her pregnancy successfully up to term delivering a healthy baby through C-section for obstetrical indication.

DISCUSSION

The patho physiological mechanism of the OHSS is not fully explained. It seems to depend on the release of vasoactive substances secreted by the ovaries, causing mesothelial hyperpermeability with fluid leakage from the intravascular to the extravascular space, therefore, generating a massive third space loss. The crux constitutes an equilibrium between proangiogenic and antiangiogenic factors found in follicular fluid (4).The loss of fluid and protein into the abdominal cavity generates hypovolemia and hemoconcentration responsible for blood circulation disorders and renal function. The most severe complications are the result of hypercoagulability and decreased renal perfusion.

In most cases, the OHSS results from administration of exogenous gonadotropins for infertility treatments. However, in some circumstances, this syndrome occurs in the absence of such treatment. A number of authors suggest that this syndrome occurrence is more frequent in cases of polycystic ovary syndrome, hypothyroidism, twin pregnancy and molar pathology (3). In our case patient had primary hypothyroidism.

The condition was first described by Rothmensch and Scommegna in 1989 in a hypothyroid woman (5) and suggested a causal link between spontaneous OHSS and hypothyroidism . The second case was reported by Zalel et al in 1992 (6) in which PCOS was found to be the underlying cause for the development of this syndrome in response to endogenous leutinizing hormone and hCG surge. In 1996 Ayhan et al. (7) reported a third case of spontaneous OHSS with 12 weeks pregnancy where absence of any underlying cause led to suspicion of malignancy and surgical intervention. The condition resolved subsequently and a retrospective diagnosis of spontaneous OHSS was made. Olantunbosun et al in 1996 (8) reported spontaneous OHSS in 4 consecutive singleton pregnancies in a patient of PCOS .

Spontanoeus OHSS associated with hypothyroidism has been reported by Ahmed Kamel et al (2010) and Smisha Sridev et al (2013). Cordoso et al. reported a case of spontaneous OHSS and primary hypothyroidism where TSH level and ovarian size returned to normal at 24 weeks of gestation [9,10,11].

Edwards-Silva et al. (12) reported a case of pregnancy with spontaneous OHSS with uncontrolled hypothyroidism and deep vein

thrombosis in a Rh isoimmunised pregnancy which was managed conservatively with levothyroxine and heparin and noted regression of ovaries by 22 weeks of gestation after adequate thyroid repletion and delivered a non-hydropic preterm baby at 35 weeks of gestation.

In 2003 Smits et al.(13) identified a mutation in FSH receptor gene in a patient presenting spontaneous OHSS in each of her 4 pregnancies. Same mutation was found in the patient's sister who similarly presented with spontaneous OHSS during her pregnancy.

De Leener (14) classified OHSS into three types based on clinical presentation and FSH receptor mutation. Type I is associated with the mutated FSH receptor and this type may cause recurrent spontaneous OHSS. Type II is secondary to high levels of human chorionic gonadotropin (hCG) as in hydatiform mole and multiple gestation and is most frequent one. Type III is related to hypothyroidism.

The pathophysiology of spontaneous OHSS associated with hypothyroidism is not studied well.The explanations given are (a) excessive estriol via 16-hydroxylation pathway instead of normal 2-hydroxylation that has been demonstrated in hypothyroid patients. Excessive gonadotropin release due to decreased feedback regulation caused by substitution of estradiol by less potent estriol would result in spontaneous OHSS in those subjects;(b) High levels of thyroid stimulating hormone can directly stimulate ovaries in women with hypothyroidism and cause ovarian hyperstimulation. (15).

Spontaneous OHSS has been reported besides normal singleton pregnancies that included a triplet pregnancy (Nisha Rani et al. 2012), missed abortion (Bibi Shahnaz Ali et al. 2008) and partial hydatidiform mole with fetal and placental triploidy (M. Ludwig et al. 1998). [16,17,18]

Thus even though extremely rare there have been spontaneous OHSS cases reported all over the world in various clinical settings.All the cases reported emphasize on the need for maintaining a high index of suspicion so as to prevent fatal complications due to delay in management and to avoid unnecessary surgical intervention . In this case due to high index of suspicion and an early diagnosis with prompt management on lines of OHSS, the pregnancy could progress to term with a positive outcome.This case re-emphasises the causal links between hypothyroidism and spontaneous OHSS.

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