Pregnancy complicated by spontaneous ovarian hyperstimulation syndrome and hyperthyroidism

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Abstract
Ovarian hyperstimulation syndrome (OHSS) is a potentially life-threatening complication associated with ovarian induction. OHSS is a very rare event in spontaneous pregnancies, most often in situations of multiple or molar gestations, hypothyroidism or polycystic ovary syndrome. We describe a patient with naturally conceived pregnancy associated with spontaneous OHSS complicated by hyperthyroidism. The patient was admitted at 17 weeks of gestation with abdominal pain because of bilateral multilobulated cystic ovaries to the Chair and Department of Obstetrics and Perinatology of Medical University of Lublin. The woman was treated with antithyroid drug and successfully delivered at 36 weeks of gestation.

Key words: spontaneous ovarian hyperstimulation syndrome, pregnancy, hyperthyroidism

Introduction
Ovarian hyperstimulation syndrome (OHSS) is a rare iatrogenic complication of ovarian stimulation that occurs during either the luteal phase or early pregnancy [1]. It has been described to arise after treatment with exogenous gonadotropins, clomiphene citrate and gonadotropin-releasing hormone agonists [1, 2]. Women without any pharmacological intervention are hardly ever diagnosed with spontaneous OHSS [3,4]. Patients with polycystic ovaries are more sensitive to the endogenous gonadotropins and more likely develop OHSS [2,5]. The association of OHSS and endocrinopathies in pregnant women may create a clinical problem. We describe a case of spontaneous OHSS in a patient who became pregnant naturally and suffered from hyperthyroidism.

Case presentation
A 38-year-old woman, gravida 3, was admitted to the Chair and Department of Obstetrics and Perinatology of Medical University of Lublin at 17 weeks of gestation with abdominal pain, nausea and vomiting. She had a history of two unremarkable normal pregnancies. The patient conceived spontaneously and denied having ever taken any ovulation inducing agent. Hyperthyroidism was reported six years before but antithyroid therapy was ended two years later.

Vomiting, nausea and abdominal disturbances started at 10 weeks of gestation and increased up to admitting to our unit.

Based on her history of endocrinopathy, thyroid function was measured. Thyrotropin (TSH) was < 0.04 mIU/l (reference range 0.4-4.9 mIU/l), free triiodothyronine (FT3) 33.2 pmol/l (3.0-7.0 pmol/l) and free thyroxine (FT4) 76.4 pmol/l (12.0-22.0 pmol/l). Treatment with 150 mg propylthiouracil per day was started.

Abdominal and pelvic ultrasound examination confirmed a single, normal intrauterine pregnancy of 17 weeks and bilaterally enlarged multicystic ovaries measuring 120 × 108 mm on the right and 120 × 117 mm on the left (Fig. 1). Placenta was normal. There was no fluid in the cul-de-sac.

The levels of human chorionic gonadotropin (hCG) were markedly elevated between 16 and 19 weeks of gestation. Serum levels of hCG were 609.964 mIU/ml (normal values: 5.730-54.585 mIU/ml), 548.883 mIU/ml (5.267-57.465 mIU/ml), 458.111 mIU/ml (3.180-51.360 mIU/ml) and 442.763 mIU/ml (5.879-55.183 mIU/ml) at 16, 17, 18 and 19 weeks of gestation respectively. No signs of virilization were observed.

A complete blood count, electrolytes, liver function and coagulation profile gave results within normal limits. A chest x-ray revealed no abnormalities. Conservative management consisted of bed rest, close monitoring (blood pressure, pulse and urinary output) and antithyroid therapy. Ultrasound-guided fine needle aspiration of the largest ovarian cysts (400 ml) was performed at 18 weeks of gestation because of increasing abdominal pain. The procedure was repeated at 21 weeks of gestation and 200 ml of fluid was obtained. No compli-
cations were observed. Aspirated fluid was negative for malignant cells, bacteria and fungi.

Fig. 1. Ultrasound examination of left ovary

During therapy, at 26 weeks of gestation thyroid function was normalized (TSH 0.04 mIU/l, FT3 16.5 pmol/l, FT4 5.4 pmol/l). Treatment with propylthiouracil (100 mg/day) was continued. Ultrasound examination performed at 20 weeks of gestation showed normal fetal growth and reduction of left ovarian size to 64 x 36 mm and right to 33 x 24 mm.

At 36 weeks of gestation the patient went into labour and underwent an uncomplicated vaginal delivery of male newborn weighing 2340 g, but showed hypospadias. Histological examination showed normal placenta. The hCG level at delivery was 4 mIU/ml and ultrasound examination revealed normal ovaries.

Discussion

Spontaneous OHSS is very infrequent and is always reported during pregnancy. Only a few cases have been described in singleton gestation [2, 5-10]. Some of them were associated with primary hypothyroidism [3, 4, 11]. A series of cases of recurrent OHSS can be found in the literature [5, 8, 12].

The woman referred to us conceived spontaneously. Previous two pregnancies were normal; she was never diagnosed polycystic ovarian syndrome. Abdominal pain, nausea, vomiting started at 10 weeks of gestation were reported by other authors [3, 5, 6]. On account of the fact that she had weight loss, distress, palpitations, tachycardia and a history of thyroid dysfunction, thyroid hormones were measured. Laboratory data showed hypothyroidism. Because normal values of TSH were associated with very high FT3 and FT4 levels, hCG was checked. Markedly elevated hCG noted in our case can usually be connected with multiple gestation, molar pregnancy, choriocarcinoma or various germ cell tumors [13, 14]. In our patient ultrasound examination showed singleton gestation with normal fetus and placenta.

Similar findings were noted in cases classified as hyperreactio luteinalis [15]. That uncommon condition complicating pregnancy is characterized by ovarian enlargement caused by presence of multiple luteinized follicular cysts formed in response to hCG stimulation and is usually observed in the third trimester of pregnancy. The clinical presentation of hyperreactio luteinalis can mimic OHSS, but this syndrome is observed in the first trimester [16]. Virilization is seen in up to 25% of patients [15]. Our patient developed her signs in the second trimester and no androgenization was observed.

High levels of hCG are not observed in all cases of OHSS [2, 17]. In hypothyroid women, elevated concentrations of TSH may stimulate follicular growth and mediate OHSS because of the presence of nuclear thyroid receptors in the granulosa cells [4, 10, 11, 18]. The casual relationship between hypothyroidism and OHSS is suggested by the constant regression of the ovarian cysts after the institution of thyroid hormone replacement therapy [3]. In contrast to cited reports, our case shows appearance of hyperthyroidism. Ludwig et al. [14] suggested that hyperthyroidism which occurred neither before nor after pregnancy in their patient with a partial hydatidiform mole and a triploidy of the fetus was due to the high hCG concentration and spontaneous OHSS. It has been shown recently that hCG was able to stimulate TSH and FSH receptors in vitro in conditions that mimic high ligand concentrations [19-22]. It seems probable that identification of hypothetical mutation in receptors of glycoprotein hormones, i.e. hCG, LH, FSH and TSH, could help us to explain the problem of coexisting hyperthyroidism and spontaneous OHSS in our patient [19, 23].

Women with OHSS require treatment consisting of bed rest, close monitoring and fluid therapy. In connection with the fact that our patient’s symptoms, i.e. nausea, vomiting, abdominal distension, enlarged ovaries and neither ultrasound nor clinical evidence of ascites corresponded to grade 2 of OHSS according to the classification proposed by Golan et al. [24]. Absence of haemoconcentration in our patient may be due to the counter-acting effect of haemodilution in pregnancy.

Aspiration of the large cysts was done under ultrasonographic guidance twice during pregnancy in our patient. Abu-Louz et al. [17] noted decrease of ovarian and abdominal pain after ultrasound-guided needle aspiration. Additionally, histological examination of aspirated fluid can have important consequences for diagnosis and

Our case, as well as literature data [3], indicates the importance of assessing thyroid function in women with OHSS.

References