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آموزش مهارت های کاربردی در تدوین و چاپ مقاله
Spontaneous ovarian hyperstimulation in pregnant women with hypothyroidism

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Spontaneous hyperstimulations syndrome had been reported in women with hypothyroidism, and polycystic ovary syndrome. This report describes a case in which a naturally conceived pregnancy was associated with spontaneous ovarian hyper stimulation and hypothyroidism.1-4

We treated our case by levothyroxine. Within 2 weeks a remarkable improvement was observed, with resolution of ascites and decrease in serum TSH level. The hormonal tests for thyroid function were normal 3 months after treatment. Pregnancy was allowed to proceed under close maternal and fetal surveillance.

The mother’s progress was then followed at normal antenatal check-ups and no serious complications developed. Ten weeks after delivery ovarian cysts regressed completely. Thyroid hormone replacement seems to be the best therapeutic approach, but in some patients the complete resolution of the ovarian cysts does not take place after being euthyroid.

Key Words: Hypothyroidism, Spontaneous ovarian hyperstimulation, Pregnancy

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Introduction

Ovarian hyperstimulation syndrome (OHSS) has been extensively described after treatment with exogenous gonadotropins, clomiphene citrate, and gonadotropin releasing hormone. OHSS, not related to ovulation induction is rare. Spontaneous hyperstimulation syndrome has been reported in women with hypothyroidism, polycystic ovary syndrome and pregnancy), gonadotroph pituitary adenoma, and normal pregnancy.1,4

This report describes a case in which a naturally conceived pregnancy is associated with spontaneous ovarian hyper stimulation and hypothyroidism.

Case report

A 30 year-old gravid 1, was admitted at 20 weeks’ gestation because of abdominal pain and distension. The current gestation started spontaneously, and no medications had been taken by the patient during the preceding months. On admission physical examination detected mild tenderness and distension of lower abdomen. Pelvic examination found bilaterally enlarged cystic ovaries, and a pregnancy of 20 weeks gestation.

Abdominal ultrasound showed a 20-week singleton normal pregnancy; there were bi lateral
Spontaneous ovarian hyper stimulation in hyper thyroidism

Fig. 1. Bilateral multiloculated ovarian cysts

multiloculated ovarian cysts with diameters of 20×16 cm (right ovary) and 16×10 cm (left ovary) and mild ascites. The placental appearance was normal (Fig.1). Doppler ultrasonographic studies were normal. Laboratory testing revealed normal hemoglobin and hematocrit; platelet count, leukocyte count, blood urea nitrogen, and creatinine. The serum levels of beta-human chronic gonadotrophin (β-hCG), antithyroglobuline, and antiperoxidase were normal.

TSH concentration was increased (400 U/mL). Table 1 summarizes the results of the hormonal tests performed. With these findings, the diagnosis of mild spontaneous ovarian hyper stimulation associated with a singleton intrauterine pregnancy and hypothyroidism was made.

Treatment given was of bed rest, close monitoring of blood pressure, pulse rate, urine output, hematocrit, electrolytes, coagulation profile, and fluid therapy.

Based on the diagnosis of hypothyroidism, associated with ovarian hyper stimulation syndrome, treatment with levothyroxine100μgr/day was instituted, with a progressive dose increase that reached 200μgr/day. Within 2 weeks, remarkable improvement was observed, with resolution of ascites and gradual reduction of ovarian size. The patient was discharged after 2 weeks and her. The patient’s condition was monitored weekly for 1 month, after which her progress was followed in intervals with at normal antenatal check-ups. Fetal growth rate and amniotic fluid were normal, and no morphological fetal abnormalities were seen.

By 34 weeks, TSH returned to normal, and on transabdominal ultrasound the ovarian cysts were seen to have decreased in size to 15 cm ×8 cm and 13 cm ×8 cm, right and left ovaries, respectively.

Treatment by levothyroxine was continued and clinical and laboratory follow up with control were periodically carried out up to 38 weeks. Eighteen weeks after starting levothyroxine treatment, follow up ultrasonography failed to show marked reduction in the size of her ovaries. At 38 weeks, the size of ovarian cysts was unchanged and the fetus was in breech presentation, leading to a decision for laparotomy and cesarean section, both for diagnosis and treatment. The patient gave birth to a healthy, normal female baby of 3200 g of 38 weeks' gestation. Aspiration of a large ovarian cyst and wedge biopsy was done in laparotomy.

Intraoperative histological examination of frozen section from the ovaries revealed benign cysts. Ten weeks after delivery, pelvic ultrasound showed normal size ovaries.
Table 1. Hormonal tests results

<table>
<thead>
<tr>
<th>Biochemical tests</th>
<th>Results</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid-stimulating hormone (µU/mL)</td>
<td>&gt;400</td>
<td>0.47-5</td>
</tr>
<tr>
<td>Triiodothyronine (ng/mL)</td>
<td>0.28</td>
<td>80-200</td>
</tr>
<tr>
<td>Thyroxine (ug/dL)</td>
<td>0.6</td>
<td>9.1-23.8</td>
</tr>
<tr>
<td>Free triiodothyronine (pg/mL)</td>
<td>1.1</td>
<td>2.2-5</td>
</tr>
<tr>
<td>Free thyroxine (ng/dL)</td>
<td>0.4</td>
<td>0.7-1.8</td>
</tr>
<tr>
<td>CA-125 (U/mL)</td>
<td>39</td>
<td>≤35</td>
</tr>
</tbody>
</table>

Discussion

Ovarian hyperstimulation syndrome usually occurs in association with ovulation induction, but the physiopathologic mechanisms are poorly understood.

Spontaneous OHSS is usually associated with PCOS, Down’s syndrome, hypothyroidism and multiple pregnancy.1-4 In our case, hypothyroidism was diagnosed at 20 weeks’ gestation of a pregnancy conceived spontaneously. This case suggests a possible relationship between spontaneous ovarian hyperstimulation and primary hypothyroidism.

The causal relationship between hypothyroidism and ovarian hyperstimulation is suggested by the consistent regression of the ovarian cysts after the institution of thyroid hormone replacement therapy; this did not happen in our patient, in whom resolved several weeks after delivery. The association of spontaneous OHSS with hypothyroidism has been described in three case reports.1-3 In women with hypothyroidism, the elevated concentrations of thyroid-stimulating hormone may mediate an ovarian hyperstimulation because of the presence of nuclear thyroid receptors (TR and TRβ) in the granulosa cells. In the above mentioned studie the hormonal tests for thyroid function and ovarian size were normal, 3 months after treatment. As the exact pathogenesis of OHSS is unknown, treatment relies on an empirical and symptomatic approach.5 In cases treated by medical management, which was used for our case the complete resolution of the ovarian cysts takes almost 3 months. Within 2 weeks a remarkable improvement was observed, with resolution of ascites and decrease in TSH. TFTs were normal 3 months after treatment. Pregnancy was allowed to proceed under close maternal and fetal surveillance. Mother’s progress was then followed at normal antenatal check-ups and no serious complications developed. Thyroid hormone replacement seems to be the best therapeutic approach in patients,1-4 but in our case the ovarian cysts did not regress completely after 4 months of thyroid replacement therapy. While surgical management of spontaneous OHSS increases the risk of abortion, it simultaneously shortens the period in which most serious complications develop.

However, surgical management is only advocated for cases of follicular rupture, cyst hemorrhage or, torsion of the ovary.6,7 Since medical treatment for 18 weeks did not significantly resolve the ovarian cysts, it was decided to proceed with an exploratory laparotomy during cesarean section. Intraoperative histological examination of frozen sections from the ovaries revealed benign cysts. Aspirations of the large ovarian cysts were done in order to avoid the probable serious complications of the remaining cysts. Cyst aspiration during pregnancy is recom-
mended by some clinicians, and should be judged against the risk of bleeding of fragile ovaries that could lead to oophorectomy. Articles on OHSS, advise that surgery should be conservative, with a minimum of invasive manipulation in order to preserve ovarian integrity as much as possible as eventual spontaneous restoration to normal size is inevitable.

Comment
Thyroid hormone replacement seems to be the best therapeutic approach, but in some patients the complete resolution of the ovarian cysts fails to occur after 3 months. In cases of spontaneous OHSS associated with pregnancy and hypothyroidism, conservative surgery should be the first approach when ovarian cysts persist in spite of adequate medical treatment. It is suggested that a longer observational management without surgical intervention be considered in some proper cases of OHSS if there is no other indication for laparotomy.

References
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