Increased concentrations of renin, aldosterone and Ca\textsuperscript{125} in a case of spontaneous, recurrent, familial, severe ovarian hyperstimulation syndrome

CASE REPORT

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We report for the first time increased concentrations of aldosterone and renin in a case of spontaneous, recurrent, familial, severe ovarian hyperstimulation syndrome (OHSS). High concentrations of Ca\textsuperscript{125} were also found. Our patient was a 26 year old woman, gravida 2, para 1, affected by severe OHSS, who denied having ever consumed any ovulation drug. Both the patient and her only sister had suffered from a similar condition in their previous pregnancies. The patient was treated with i.v. fluid therapy. Paracentesis was performed on one occasion. The patient was dismissed after 25 days in good condition. Blood count and blood chemistry confirmed the severity of the clinical picture. We conclude that spontaneous OHSS, although very rare, may have been underestimated so far. It can be recurrent and may also be familial. The intra-ovarian prorenin–renin–angiotensin system may play a role in its aetiopathogenesis.

Keywords: aldosterone/Ca\textsuperscript{125}/ovarian hyperstimulation syndrome/renin

Introduction

Ovarian hyperstimulation syndrome (OHSS) is a well-known potentially life threatening iatrogenic complication of ovulation induction (Brinsden et al., 1995).

The spontaneous occurrence of OHSS has been reported in a hypothyroid patient with Down’s syndrome (Rotmensch et al., 1989), in a spontaneous singleton pregnancy in a healthy woman (Rosen and Mitchell, 1991) and in a spontaneous singleton pregnancy in a patient with polycystic ovarian disease (PCOD) (Zalel et al., 1992). The recurrence of a second spontaneous OHSS has also been reported in the same patient with PCOD (Zalel et al., 1995). More recently, three other cases of spontaneous OHSS have been reported (Ayhan et al., 1996; Lipitz et al., 1996; Regi et al., 1996).

We report a case of spontaneous, recurrent, familial OHSS. Moreover, we report high concentrations of renin and aldosterone in such circumstances.

Case report

The patient was a 26 year old woman, gravida 2, para 1. She was admitted to our department because of nausea, vomiting, shortness of breath and complaints of abdominal fullness at 10 weeks gestation.

In her only previous pregnancy, the patient had been admitted to our department at 10 weeks gestation, for lower abdomen pain, vomiting and nausea. An ultrasound scan revealed bilateral multilobulated cystic ovaries, occupying the whole pelvis, and a viable pregnancy. Laboratory testing revealed haemocencentration (haemoglobin 14 g/dl; haematocrit 46%). The patient was treated with i.v. fluid therapy (consisting of Ringer lactate, 500 ml, plus albumin 25%, 50 ml, twice a day for 9 days, and Ringer lactate, 500 ml, plus albumin 25%, 50 ml, once a day for the following 6 days) and carefully monitored. She was discharged after 15 days with partial resolution of the symptomatology.

The patient’s sister, during her only pregnancy, had been admitted to another hospital at 11 weeks gestation for lower abdominal pain, vomiting, nausea and shortness of breath. An ultrasound scan revealed the classical picture of hyperstimulation, with enlarged cystic ovaries measuring 13×14×10 cm (right ovary) and 12×12×10 cm (left ovary), a small amount of ascitic fluid and a viable pregnancy. The patient was treated with i.v. fluid therapy (consisting of NaCl 0.9%, 500 ml, twice a day for 3 days and Ringer lactate, 500 ml, plus albumin 25%, 50 ml, once a day for 7 days) and non-steroidal anti-inflammatory drugs. In addition, two of the largest cysts were also aspirated during a laparotomy performed for suspected torsion.

Both the patient and her sister denied having ever taken any ovulation inducing agent. The past medical history of both sisters was otherwise unremarkable.

According to an ultrasound scan performed before the pregnancy at age 22 years, and the presence of regular menstrual cycles, as well as the absence of hirsutism, acne, seborrhoea and obesity, the possibility that the patient had been affected by polycystic ovary syndrome could be ruled out.

Physical examination of the patient, performed at admission, revealed normal temperature (36.5°C), and blood pressure (120/70 mmHg), with tachycardia (100 beats/min). The patient appeared dehydrated and dyspnoeic. The abdomen was distended and tense with clear signs of ascites.

Pelvic ultrasound examination revealed multilobulated, cystic ovaries measuring 11×10×9 cm (right) and 13×11×10 cm (left), a large amount of ascitic fluid, and a viable intrauterine pregnancy whose size was consistent with dates (Figure 1).
Figure 1. Pelvic ultrasound scan of a 26 year old pregnant patient with ovarian hyperstimulation syndrome (10 weeks gestation). The scan shows ovarian cysts and a gestational sac with an embryo and ascitic fluid.

Table 1. Laboratory values at admission (normal values for a 10 week pregnancy have been provided by our laboratory)

<table>
<thead>
<tr>
<th>Substance</th>
<th>Value</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSH (mIU/ml)</td>
<td>0.4</td>
<td>&lt;1</td>
</tr>
<tr>
<td>LH (mIU/ml)</td>
<td>75</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Prolactin (ng/ml)</td>
<td>53</td>
<td>5–50</td>
</tr>
<tr>
<td>Progesterone (ng/ml)</td>
<td>410</td>
<td>23–54</td>
</tr>
<tr>
<td>ACTH (pg/ml)</td>
<td>8.7</td>
<td>8–130</td>
</tr>
<tr>
<td>Testosterone (ng/ml)</td>
<td>1.1</td>
<td>0.6–2</td>
</tr>
<tr>
<td>Oestradiol (pg/ml)</td>
<td>3402</td>
<td>2000–2500</td>
</tr>
<tr>
<td>Renin (ng/ml)</td>
<td>62</td>
<td>0.4–12.8</td>
</tr>
<tr>
<td>Aldosterone (pg/ml)</td>
<td>4950</td>
<td>210–900</td>
</tr>
<tr>
<td>Androstenedione (ng/ml)</td>
<td>3.7</td>
<td>1–4.5</td>
</tr>
<tr>
<td>DHEAS (µg/dl)</td>
<td>49</td>
<td>12–250</td>
</tr>
<tr>
<td>T3 (ng/ml)</td>
<td>0.6</td>
<td>1–2.5</td>
</tr>
<tr>
<td>T4 (ng/ml)</td>
<td>96</td>
<td>70–150</td>
</tr>
<tr>
<td>TSH (mU/l)</td>
<td>0.7</td>
<td>0.5–6</td>
</tr>
<tr>
<td>Ca125 (IU/ml)</td>
<td>30</td>
<td>0–30*</td>
</tr>
<tr>
<td>Ca125 (IU/ml)</td>
<td>824</td>
<td>0–35*</td>
</tr>
<tr>
<td>CEA (ng/ml)</td>
<td>0.3</td>
<td>0–4*</td>
</tr>
<tr>
<td>α-Fetoprotein (ng/ml)</td>
<td>2.2</td>
<td>0–15*</td>
</tr>
</tbody>
</table>

*Normal values in non-pregnant states.

Laboratory testing revealed: haemoglobin 16.3 g/dl, haematocrit 49%, red blood cells 5 930 000 cells/mm³, white blood cells 20 100 cells/mm³, platelets 316 000 cells/mm³, Na⁺ 129 mmol/l, K⁺ 4.9 mmol/l, albumin 2.5 g/dl.

The hormonal evaluation of the patient is reported in Table 1, together with the value of some tumour markers. High progesterone and oestradiol values were found, together with high concentrations of total renin and aldosterone. Increased concentrations of Ca125 were also observed.

During hospitalization the patient received intensive i.v. fluid therapy with NaCl 0.9%, 500 ml, plus albumin 25%, 50 ml, once a day for 11 days and Ringer lactate, 500 ml, twice a day plus albumin 25%, 50 ml, once a day for 10 days.

In order to relieve breathing difficulty and severe discomfort due to tense ascites, paracentesis was performed on one occasion under ultrasound guidance. Two litres of ascitic fluid were removed in 6 h.

The patient was dismissed after 25 days, with complete resolution of the clinical picture and normalization of the laboratory parameters. She subsequently delivered a healthy baby at term.

Discussion

Seven cases of spontaneous OHSS have been reported in the literature so far. In one case the patient was hypothyroid (Rotmensh et al., 1989), while two other reports described the same patient affected by PCOD (Zalel et al., 1992, 1995). In our case, both these conditions could be ruled out.

The elevated concentrations of Ca125 that we found in our patient have already been observed in spontaneous OHSS (Rosen and Mitchell, 1991; Lipitz et al., 1996). Indeed, elevated concentrations of this marker are a common finding in pregnancy and OHSS following ovulation induction (Jager et al., 1987). Moreover, all the processes that irritate the peritoneum increase the concentrations of Ca125. In our patient, peritoneal irritation, pregnancy and OHSS may all have acted synergistically in causing the dramatic increase in Ca125 concentrations that we observed.

We also report elevated total renin and aldosterone concentrations in a spontaneous OHSS. Indeed, increased concentrations
of these hormones have been reported in OHSS following ovulation induction and the severity of OHSS correlates with plasma renin activity (Navot et al., 1987). In these cases, elevation of plasma renin activity and aldosterone concentrations have been demonstrated in the presence of clearly expanded plasma volume (Ong et al., 1991). This suggests that activation of the renin–angiotensin–aldosterone system is a primary event in the pathogenesis of OHSS and not a consequence of plasma volume reduction. Our observation of elevated plasma renin and aldosterone concentrations in the absence of previous administration of ovulation inducing drugs, further supports a pivotal role of intra-ovarian prorenin–renin–angiotensin system in the genesis of this condition. On the other hand, Balasch et al. (1994) have recently reported a close correlation between plasma renin activity and other volume dependent endogenous vasoactive substances (such as noradrenaline and antidiuretic hormone) in OHSS. Their observation suggests that baroreceptor-mediated stimulation of the sympathetic nervous system secondary to circulatory dysfunction may be the key point in the increase of plasma renin activity in OHSS. Indeed, in our case, the reduction in plasma volume might have stimulated the circulating renin-angiotensin system. Moreover, a stimulating role for the high plasma concentrations of progesterone and oestradiol on the circulating renin-angiotensin system. Nevertheless, a stimulating role for the high plasma concentrations of progesterone and oestradiol on the circulating renin–angiotensin system has also been recently demonstrated (Sealey et al., 1994).

Our report also suggests that spontaneous OHSS may be a familial condition. Although anecdotal, our observation indicates that genetically determined factors may be implied in the aetiology of this condition. To our knowledge, there is no report of an increased incidence of OHSS following ovulation induction among members of the same family. However, our report points out that the presence of an affected sibling could be considered a risk factor for developing OHSS.

Although the occurrence of spontaneous OHSS has to be considered an extremely rare condition, our experience suggests that its incidence may have been underestimated so far. Indeed, our patient and her sister had previously suffered spontaneous OHSS and had been treated without performing any investigation on the possible cause of the condition.

Moreover, similar cases of spontaneous OHSS, when admitted to a surgical emergency department, may undergo surgical treatment by medical staff with no experience in reproductive medicine. With the increasing awareness of these conditions, more and more cases could be detected and reported.

**References**


*Received on January 17, 1997; accepted on July 10, 1997*